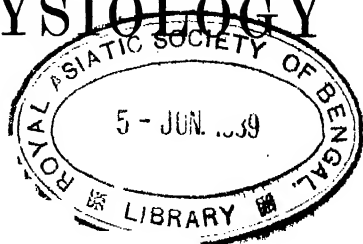


ELECTRO-PHYSIOLOGY



ELECTRO-PHYSIOLOGY



BY

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TRANSLATED BY FRANCES A. WELBY ✓

WITH ONE HUNDRED AND THIRTY-SIX FIGURES

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Dedicated in Gratitude

TO

PROF. DR. EWALD HERING

MY VENERATED MASTER

PREFACE

FROM the very beginning of Experimental Physiology, the marvellous action of electrical currents upon excitable animal tissues, and the electrical forces which, under certain conditions, proceed from these tissues themselves, have again and again attracted the attention of scientific men, and have given rise to a vast number of experiments, which at the present day are still being prosecuted in all directions. This is accounted for by the great significance at first attributed to the action of electrical forces in the living organism. And at a later period, when these anticipations had not been fully realised, and the desired goal of a "physical" explanation of muscular contraction, nerve conductivity, etc., seemed farther off than ever, the multitude of facts meantime discovered, together with the exactness of the methods of observation, and the conviction that perseverance in the familiar path must eventually lead to the solution of some at least of the countless problems of living matter, spurred the student on to renewed endeavour. Moreover, there was a growing desire to establish the many and successful applications of electricity in clinical medicine on a firm and secure basis, and to found an exact science of electro-therapeutics. Thus it has come about that the literature of Electro-Physiology, in a wide sense, has swollen to a bulk that practically debars any student who is not a specialist from critical acquaintance with it.

Fifteen years have elapsed since the last review of the subject by Hermann, in his *Handbuch der Physiologie*—an interval sufficient, after the rapid advances in this department, to make a new account desirable. The monographs are so scattered, and in some cases so little accessible, that it is difficult to obtain a synopsis of them. I have worked so long and zealously at this particular department, and have in preparation for my Lectures acquired a familiarity with its literature (which might otherwise have escaped me), so great, that at last I believe myself justified in venturing on the experiment of giving a comprehensive survey of Electro-Physiology—a task in which I am only too well aware of my shortcomings. Notwithstanding, I venture to hope that I have rendered a service, not merely to many of my colleagues, but also perhaps to a portion of the medical public, since I have aimed at a connected review of fundamental *facts*, and have only introduced details of experimental method, and pure theory, where they were indispensable to an understanding of the subject. The chapter on Electrical Fishes in particular is commended to the indulgence of my fellow-workers; it could only be compiled from the results of others, as I have no first-hand experiences to draw upon. Those who know its widely-scattered literature must condone the defects of the present attempt, in view of the lack of any other summary. As an excuse for the size of the work I may state that it has grown out of my lectures, and could only thus escape a certain pedagogic dryness. In justification of the sections treating of Histology and General Physiology, I may be allowed to point out the intimate relations between structure and function in muscle, nerve, and electrical organs, as well as, on the other hand, the necessity of premising the discussion of more special questions, with the general conditions and forms of manifestation of activity in irritable tissues. Hence it seemed to me not merely desirable, but imperative, to

treat these relations more fundamentally than is usual in physiological publications. All this has contributed to expand the book, perhaps unduly, beyond its natural limits. Again, it may be objected that the whole survey is taken from one definite standpoint, so that individual chapters are perhaps treated in too one-sided a fashion. But I frankly confess to having thought less of avoiding a subjective tinge by the elimination of every partisan consideration, than of showing how the phenomena range themselves under that point of view from which I formerly learnt to judge of them from my venerated master, Hering.

In dedicating this book to him as an unworthy token of my esteem and gratitude, I am well aware that I am only giving back what I formerly received from him.

JENA, *November* 1894.

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INTRODUCTION

ELECTRO-PHYSIOLOGY, as set forth in the following pages, comprises on the one hand the theory of the electrical excitation of excitable tissues, on the other the electromotive reactions which these exhibit. In order to understand the subject, an adequate knowledge of the phenomena of excitation, and in particular of the effects of current upon living matter, is essential, and must therefore be considered in the first instance. While in Morphology it is a matter of course that any inquiry should proceed from simple to complex, in Physiology experience and intuition alike teach us that the converse is often more fertile and more expeditious. This is due in part to the nature of the methods at our command, in part to fundamental physiological differences in the individual elements. What is morphologically simple is not always physiologically intelligible; in a sense we might rather affirm the opposite. If it be true that every function of the more highly-developed multicellular organism is potentially nascent in the relatively undifferentiated protoplasm of the amœba, the apparent simplicity of the latter must conceal a complex of physiological activities not to be compared with those cases in which one kind of cell serves only one single function, as a muscle-cell contraction, a gland-cell secretion, etc.

Here we have obviously a better chance of acquiring exact knowledge of the inherent qualities of the physiological function in question than if we turn to primitive organisms whose protoplasm serves indifferently the most diverse functions. The study of glands and gland-cells reveals more of the process of secretion than the investigation of the same process in unicellular organisms, and the physiology of muscle has added more to our knowledge of contraction and its connected processes than we could ever have

learned from microscopic examination of lower organisms. It is for this reason that **muscle**, the most highly differentiated form of contractile tissue, has been selected as the point of departure in the following attempt at a comprehensive survey of Electrophysiology.

CHAPTER I

ORGANISATION AND STRUCTURE OF MUSCLE

EVEN at a low grade of differentiation there is a wide range of **Fibrillated Structures** in contractile protoplasm, and the great significance of this organisation for the contractile process and motor phenomena of protoplasmic substance is unmistakably attested by the behaviour of ciliated cells, and of spermatozoa in particular.

Without entirely subscribing to the theory recently brought forward by Balloitz (1) and others, "that all regular, definitely canalised contractions of contractile substances denote the presence of regular, parallel, or approximately parallel fibres" (against which there is much counter-evidence), it is nevertheless remarkable that *a fibrillated structure of protoplasm is more or less unequivocally present in nearly every case of energetic, and especially of rapid, contraction.* This is expressed most clearly in the highest differentiated forms of contractile animal protoplasm, *i.e.* **Muscle-fibrils, Muscle-cells, and Muscle-fibres.**

It appears to be of fundamental importance, as well morphologically as physiologically, to the conception of "*muscle*" that structures which, in virtue of organisation and function, may properly be termed muscular, first appear as single and isolated, or fasciculated, **fibrils.** This is as true of ontogenetic as of phylogenetic development. On examining the latter, we encounter the first genuine muscles in some of the ciliated Infusoria, for it is at least doubtful whether the delicate and swiftly contracting protoplasmic threads of certain fresh-water Heliozoa (*Acanthocystiden*), which Engelmann (2) calls "myopodia," or the analogous structure of many Radiolaria, the "myophrysken" of Haeckel, are true muscle-fibrils. In either case we may assume, with Engelmann,

that these structures are transitional stages between pseudopodia and muscle-fibrils proper.

If we examine a large transparent *Vorticella* under the high power, it is easy to detect delicate, converging fibrils just below the surface; they run parallel with the axis of the body, and are often finely varicose. Here we undoubtedly have a differentiation product of the ectoplasm (Fig. 1), whether—with Bütschli (3)—we regard these fibrils merely as a longitudinal series of cells within the otherwise alveolar protoplasm, or as a special structural arrangement. These fibrils (*myonema*) converge towards the junction of the stalk, there, in most cases, uniting into a cylindrical



FIG. 1.—*Corchestum polygynum*.
(Bütschli.)

filament, which appears fibrillated throughout in optical transverse section. Certain of the Heterotricha (*Stentor*, *Spirostomum*) and Holotricha (*Holophrya*, *Prorodon*, *Opaliniden*) are characterised by a much more pronounced development of muscular fibrils. Those of *Stentor*, isolated by Engelmann, were as much as 1μ in diameter. There were even indications of a finer structure, *i.e.* a kind of transverse striation (3, p. 1000).

Lieberkühn recognised the fibrils of *Stentor* as contractile elements. He observed that while invariably straight in contracted *Stentors*, they assume an undulatory appearance as soon as the infusorium begins to lengthen, becoming elongated during relaxation. As the animal grows longer, the waves become flatter. The fibrils eventually become quite straight again, and are more and more drawn out with continued extension. In the foot, which is most protracted, they lose all separate identity; in the rest of the body they resemble lines of excessive fineness. "If, as often happens, the animals shrink slowly together during several seconds, instead of contracting suddenly, the fibrils, instead of being short, thick, and straight at the maximum of contraction, will be distinctly wave-like, and not perceptibly thicker than in the ordinary extended state of the animal. The waves are often so steep and short that the fibres come into

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lateral contact. The cortical layer seems at first sight to consist of a labyrinth of crumpled fibres. When, after slowly retracting, the animals are almost globular, there is still a possibility of contraction. *Every fibril suddenly becomes short, thick, and straight.* Instead of the labyrinth of little waves there is an instantaneous reappearance of thick, straight, shining longitudinal stripes lying parallel with one another."

Stentor can apparently contract spontaneously without any assignable external stimulus. Engelmann (2, p. 447) found on applying dilute acetic acid (0.1 %), HCl (0.1 %), H_2SO_4 (4 %), etc., that single fibrils at first contracted frequently, even including those which the shrinking of the endoplasm had separated from the pellicula. Ether, chloroform, and the electric current also produce a sudden contraction of the muscular layer in the first instance. The lower threshold of stimulation differs in different forms. Stentor, e.g., reacts to much weaker currents than Carchesium. While the current is passing, the protozoans usually remain in a state of contraction, but when it is weak they relax completely after a time, even during its passage (Stentor, cf. Verworn, 4, p. 114).

All the evidence, therefore, goes to prove that there are true excitable and contractile fibrils in the myoid layer (myonema) of the Infusoria in question, and that it is the rapid shortening of these which produces the body twitches of Stentor and other Infusors. Along with these, however, there are slower contractions (as already stated), which indicate that the remaining protoplasm, which is comparatively undifferentiated, also possesses contractility in a definite direction. In these contractions the muscle-fibrils are bent up in a wavy form, and are therefore relaxed. The endoplasm cannot here play an active part, since, although contractile, it streams about in the most contrary directions, even while the animal is slowly contracting. The fact of there being many highly contractile Ciliata (*Hypotricha*), in which, nevertheless, no fibrils can be detected, proves that the differentiation of the latter is causally connected with a definite kind of movement, i.e. that muscle-fibrils subserve only rapid and energetic contractions. Of this the most salient example is afforded by the so-called "stalk-muscle" of Vorticella.

As we have seen, the fibrils at the posterior end of the body of Vorticella converge towards the neck of the stalk. In Polyps

with a contractile stalk the fibrils do not end here, but unite to form a thread-like organ, which enters the stalk, and usually runs right along it. This filament or *muscle*, almost without exception, runs down inside the sheath of the stalk in a sharp spiral. The sheath is a cylindrical tube of medium diameter, which attaches itself at the distal end to some foreign body. It has a slender, elastic wall of chitinous composition. The interior of the seemingly hollow stalk is filled with a homogeneous, vitreous, transparent mass of apparently gelatinous consistency. In *Vorticella* and *Carchesium* the filaments run through the stalk in a very elongated spiral, the number of turns varying with the length of the pedicle. According to Czermak (5) they may range from 0 to 12. In very short-stalked *Vorticellæ* there may be only $\frac{1}{2}$ —1 turn. In *Zoothamnium* the muscle-filaments do not run peripherally along the sheath of the stalk as in *Vorticella* and *Carchesium*, but lie close to the axis, surrounded on all sides by the homogeneous medullary substance, with no distinct spiral.

Since the filament is formed by the junction of the body-myonema, we may presume that it will have a *fibrillated structure*. In most forms the fibrils appear to lose their identity in the filament, and run together in a homogeneous mass. Yet this can be in appearance only, since the thick muscle-threads of certain *Zoothamnium* are distinctly fibrillated. This point will in all probability be established generally, by methods similar to those which Ballowitz employed to discover the fibrillated structure of the flagellum of the spermato-somata.

The contraction phenomena in the stalk of *Vorticella* appear to be normally sharp and sudden ("convulsive"). The contraction usually affects the whole stalk, which shrinks into a low and narrow-pitched spiral (helicoid), the turns being in close juxtaposition. The body of the animal usually contracts simultaneously with the pedicle. At times the stalk is only partially contracted, and both the upper and lower halves seem able to shrink locally, without implicating the remainder (Czermak, Kühne). The unrolling of a contracted stalk is a much slower process; it also may vary in direction, beginning, *i.e.*, from above or below, and sometimes remaining incomplete for a long period.

Czermak (*l.c.*) was the first to show that only the *filaments* of the stalk, in accordance with the function of the fibrils of the body-plasma, are the seat of contractility; it had previously been

assumed that the *sheath* of the pedicle was the contractile organ. The behaviour of Vorticellæ, whose filaments have been totally or partially destroyed, affords the clearest proof in favour of the first view. With total destruction the power of contraction is entirely abolished, with partial destruction the loss is in proportion with the injury.

The reaction of dead stalks is interesting in this connection. They are invariably contracted (*rigor mortis*), and all reagents that kill the filaments by coagulation (heat included) produce a coiling up that lasts as long as the filaments are present. When they are destroyed by decomposition, or by reagents, the stalk lengthens again. These experiments show that the elongation depends upon the elasticity of the pedicular sheath. Engelmann (*l.c.* p. 438 f.) observed in *Zoothamnium arbuscula* that the fibrils of the stalk-muscle, which in this case are quite visible, become short, thick, and straight at the moment of contraction. When relaxation begins, they lengthen again quickly, so that if the sheath of the stalk is obstructed by any accidental, external obstacle, and thus gets slowly longer, the fibrils at first present a very sinuous appearance. *The stalk-filaments of Vorticella therefore consist undoubtedly of contractile fibrils.* These observations (independently of other facts to be discussed later) seem to disprove the conjecture of Kühne (6) that it is not the filament itself, but the sheath of the filament—which he compares with what he calls the “glia” element of muscle-cells in higher animals—that is contractile, the filament (*i.e.* fibrils) being on the contrary an elastic tissue that produces extension in conjunction with the sheath of the pedicle.

Assuming the *filament* of the stalk to be the contractile element, it is easy to explain the spiral coiling and uncoiling of the latter, as was first indicated by Czermak. The stalk of the Contractilia is a cylinder with a thin, elastic wall, to the inner surface of which is attached a contractile filament descending in a steep spiral. But when a cylinder contracts along a spiral line upon its surface, it also becomes spiral.

Up to the present time there have been few attempts at artificial excitation of the stalk-muscle of Vorticella. Kühne (7) observed that Vorticella-colonies contracted suddenly when tetanised with an induction current. All the stalks remain contracted during stimulation, and it is only when the current passes

for a prolonged period that the filaments begin to expand again during tetanisation; the animals then contract only slightly from time to time, although if the current is strengthened, they can still shrink up to the junction with the bell. Headless stalks, when isolated, react in the same manner. Chemical stimuli (HCl 1 %, NH_3) also cause the stalks of *Vorticella* to contract (Kühne, *l.c.* p. 828). With a dilute solution of veratrin the stalks draw together slowly, and become intensely rigid, while the inner muscular filaments grow more highly refractive, and therefore much more visible. A very dilute solution of strychnia is equally fatal to *Vorticella*, but the phenomena are different. The animals lose their excitability, and remain passively extended, although there is a continuous ciliary movement. In this state the strongest induction shocks, as well as strong solutions of curare, fail to produce any movement (Kühne, *l.c.*)

The propagation of excitability in the muscle of the stalk should also be more exactly studied. There can be no doubt that under normal conditions spontaneous excitation, as well as contraction caused by external stimuli, spreads from the body of the vorticella. The excessive rapidity of contraction in the muscle-filament makes it indeed impossible to detect where the process begins, as it is apparently initiated everywhere at the same moment. This is the case even in the branched colonies of *Zoothamnium*, or *Carchesium*, when the whole community is retracted on mechanically exciting one individual. In *Zoothamnium* there may be direct conductivity of excitation, since every individual is a conductor to the rest through the muscular layer of its pedicle; but in *Carchesium*, where this is not the case, the convulsion communicated from one contracting individual to the next appears to be the only stimulus (Verworn, 4). In order to explain the phenomena of contraction, not merely in *Vorticella*, but in all other myoid Ciliata, it is necessary to assume that excitation can be conveyed from every point of the body-plasma to the muscle-fibrils, which are, collectively, in juxtaposition or direct connection with it; and the rate at which the excitation is propagated must be very considerable, under all conditions far exceeding that of the Rhizopoda. For if a spirostomum, or stentor, which from their elongated form are next to vorticella the best suited to such experiments, be

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excited locally, at one end only, contraction of the whole body ensues without any perceptible latent period; the difference of time, which doubtless exists in contraction of the anterior and posterior ends of the animal, being quite unnoticeable (Verworn).

THE MUSCLES OF METAZOA

In Metazoa, as in unicellular animals, the typical muscle makes its first appearance in the form of fibrils, or bundles of fibrils, in the protoplasm of certain cells. The animal kingdom exhibits an amazing variety in regard to the mass-disposition and relative arrangement of these contractile fibrils, and the formative plasma ("sarcoplasm"), of which they are a differentiation product.

In order to understand the structure and function of highly differentiated muscles, it is as important to consider their racial as their individual development, and we have next to study in detail some instructive examples of the first of these.

The simplest form of **muscle-cell** (*myoplast*¹) occurs in the epithelial muscles ("neuro-muscular cells") of the lower Coelenterata.

In Hydra, *e.g.*, the ectoderm consists mainly of large, blunt, cone-shaped, epithelial cells, the apices of which are directed inwards, and prolonged into one or more processes which form dichotomously branched fibrils bending at right angles, and running parallel to the body axis, to form collectively a sub-epithelial, contractile layer ("muscle lamella"). Accordingly in transverse section there is a small zone between the ectoderm and endoderm, in which the bisected fibrils stand out as a series of strongly refracting points.

In this case, therefore, the cell-bodies help to bound the body-surface, and, like the protoplasm of Ciliata, serve to establish relations with the external world, since they are able to receive impressions from without, *i.e.* are **excitable**. In both cases the excitation is conveyed through the protoplasm of the cell (sarcoplasm) to the contractile fibrils, and must be able to spread over large tracts of the body by conduction from cell to cell (if nerves are really wanting). The large, vacuolated, endoderm cells of

¹ In the ciliated Infusoria described above, which must be regarded as independent cell-individuals, it is, in the same connection, legitimate to speak of "cell-muscles."

Hydra, furnished with a flagellum, also possess basal muscular fibrils. A similar but more complicated arrangement exists in the Actinia. We are still in every case dealing with muscles of *epithelial* origin, *epithelial muscle-cells*, which take part in the external or internal limitation of the body-surface, or lie deep down—their epithelial origin being always, however, unmistakable. In the simplest case, a transverse section through the endoderm shows, as in Hydra, a single row of shining granules, lying under a single layer of cylindrical, epithelial cells, which it divides from the mesenchyme (Fig. 2, *a*).

Here again, as we learn from isolated preparations, we have a cross-section of muscle-fibrils (bundles of fibrils?) which must be regarded as a differentiation product of the epithelial cells. The cell-bodies are cubical, cylindrical, or filiform, according to the state of contraction of the body-wall; they carry cilia, or a solitary flagellum, at their free ends, while muscle-fibrils are differentiated off at the base, which is somewhat broader (Fig. 2, *b*). From this primitive form it is easy to derive what Hertwig (9) calls "*intra-epithelial*" muscles, in which the spindle-shaped cell-bodies are only interspersed between the epithelial cells proper, and take no part in bounding the upper surface. The "*sub-epithelial*" muscles are directly connected with these forms; they consist of long fine bands (bundles of fibrils), which only retain a thin sheet of formative plasma on the side nearest to the epithelium.

FIG. 2.—*a*, Transverse section through the muscular layer of a septum of *Sagartia parasitica*, perpendicular to the long axis of the basal fibrils; *b*, epithelial muscle-cell (isolated) of Actinia. (Hertwig.)

There can be no doubt that the nucleated mass of protoplasm here corresponds with the body of a genuine epithelial muscle-cell.

There is merely a structural difference between the last-named muscles and those bundles of muscle-fibrils which are completely surrounded by mesenchyme, and are derived from a corresponding number of myoblasts.

The individual elements in this case also are fibres (fibrils), with plasma and nucleus; but instead of lying in single juxta-

position, they unite into groups, the periphery of which is formed of the contractile fibrils, while the axis contains the corresponding nuclei and protoplasm.

Between this arrangement and the original superficial disposition of the muscle-fibrils there are numerous transitional stages, produced by involution of the muscular lamella, which obviously tends to increase the mass of the muscle with stationary body-surfaces. As long as the folding of the muscle-lamella is not excessive, the irregularities which it produces towards the free surface are equalised by the varying lengths of the epithelial cells. The supporting mesenchyme also presses from within into every fold. The involution varies considerably in degree. Sometimes "muscle-plates" are produced which stand perpendicular to the body-surface in close juxtaposition, like the leaves of a book (Fig. 3). Each leaf consists of a thin supporting lamella of mesenchyme, set on both sides with muscle-cells. It is easy to see how by such a process of involution and segregation, carried one step farther, the cylindrical fasciculi of muscles, entirely surrounded by mesenchyme, may be developed.

In Medusa we meet with conditions similar to those exhibited by Actinia. The muscle-fibrils, which are often transversely striated, everywhere exhibit a basal differentiation of ectodermal, epithelial cells, which again serve in many cases to bound the body-surface.

A structure and development of muscle, similar in many respects to that already described in Cnidaria, exists conspicuously among many Worms (*Annulata*), where the epithelial, or at least epithelioid, character of the muscle is still immediately recognisable in the simplest cases. Here the longitudinal muscle-fibres often consist of mononuclear, elongated cells, arranged like a single-layered epithelium. Each muscle-cell—isolated, or in transverse section—shows two distinctly separate substances, an internal plasmatic portion, and an external contractile substance, which again is constructed of countless smooth fibrils, running parallel with the long axis of the cell, and, as seen in cross-section, arranged in laminae lying close together, so that the contractile layer exhibits a delicate radial striation. Each single stripe corresponds



o. 8.—Transverse section of the muscles of the body-wall of *Cerianthus membranaceus*. (Hertwig.)

with a row of fibrils lying one behind the other—dotted in transverse section (Fig. 4, *B*).

The relative disposition of the contractile layer and formative plasma (sarcoplasm) varies considerably in different muscles of worms. In the simplest case each muscle is represented by an even lamina, capped by the nucleated protoplasm (Fig. 4, *B*). It is evident that this arrangement, in which the longitudinal muscular fibrils collectively form a cylindrical surface, underlying the hypodermis, corresponds with the smooth, simple, non-voluted muscular lamella of many Cnidaria. In both cases increase of mass in the contractile substance leads to a formation of folds, which in Nematode muscles may be detected in each single cell. The fibrillar layer, at first a level surface, curves into a hollow groove, opening into the coelom, and filled with formative plasma.

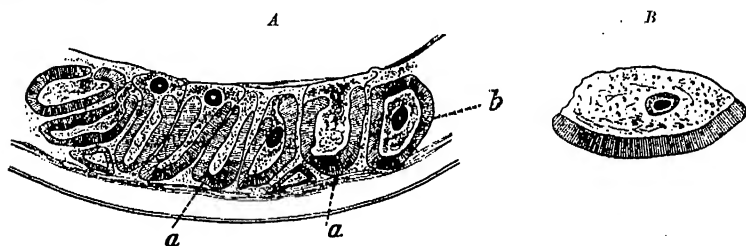


FIG. 4.—*A*, *Branchiobdella parasitica*; transverse section through the muscles of the body-wall. *a*, coelomyoid; *b*, holomyoid muscle-cells. *B*, Section through a platymyoid muscle-cell of *Ascaris lumbricoides*. (Rhode.)

Rhode (8), *e.g.*, finds in the longitudinal muscle-layer of *Branchiobdella parasitica*, every conceivable form of transition between the “platymyoid” type of muscle-cells described above, in which the fibrillated contractile stratum forms an even lamina, and the “coelomyoid” type, where the fibrillar layer has become grooved (Fig. 4, *A*, *a*).

And, again, there is but a step from these to the closed tubular muscle-cells, in which the plasma forms an axial filament sheathed on all sides by the contractile fibres. “Holomyoid” type.

The longitudinal fibres of the sheath of the cutaneous muscle of *Ascaris* are among the most interesting of the coelomyoid muscle-cells. Here the sarcoplasm is already walled in by the contractile substance at the ends of many of the muscle-cells, while in the centre the nucleated plasma (surrounded by a sarcolemma) bulges out like a hernial sac, and is often of gigantic

proportions in comparison with the fibrillar stratum (Fig. 5, *A, B*). A transverse section through the centre of such a cell

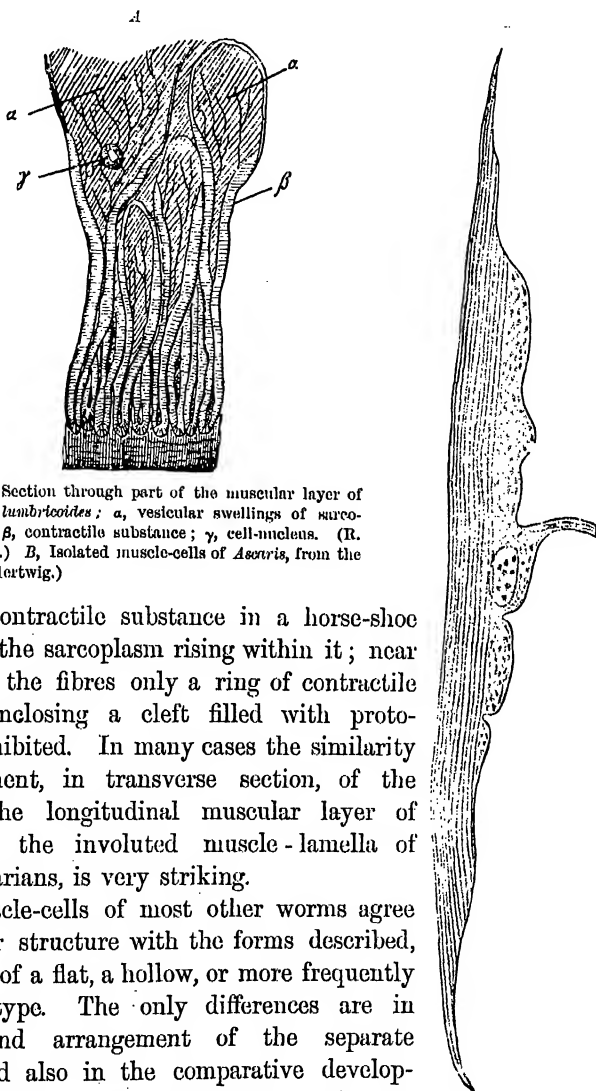


FIG. 5.—*A*, Section through part of the muscular layer of *Ascaris lumbricoides*; α , vesicular swellings of sarcoplasm; β , contractile substance; γ , cell-nucleus. (R. Leukart.) *B*, Isolated muscle-cells of *Ascaris*, from the *Bel*. (Hertwig.)

shows the contractile substance in a horse-shoe figure, with the sarcoplasm rising within it; near the ends of the fibres only a ring of contractile substance, enclosing a cleft filled with protoplasm, is exhibited. In many cases the similarity of arrangement, in transverse section, of the fibrils of the longitudinal muscular layer of worms, and the involuted muscle-lamella of certain cnidarians, is very striking.

The muscle-cells of most other worms agree in their finer structure with the forms described, being either of a flat, a hollow, or more frequently a tubular type. The only differences are in the size and arrangement of the separate elements, and also in the comparative development of volume of the sarcoplasm and contractile substance. The fibrillated structure of the contractile tissue is not always easy to distinguish, but—cf. Rhode (*l.c.*) on the musculature of Chætopoda—appears to be very generally

distributed. The several primitive fibrils are rarely detached from the formative plasma of the muscle-cell as a single layer, but are usually clustered together, and arranged in strata, which gives the appearance of radial striation above alluded to, in transverse sections of the contractile layer.

While the elaborate structure of single muscle-cells in Annulata undergoes no appreciable change as development progresses, there is on the other hand a marked variety in regard to arrangement of the muscle elements into filaments and bundles. The principle of surface growth by involution is still paramount, and just as in single muscle-cells the flat, fibrillated lamina curves round to make room for greater mass-development of the contractile substance, the same process is repeated in the grouping together of a number of muscle-cells in the longitudinal muscular layer of many Annulata.



FIG. 6.—Transverse section of body-muscles of *Lumbricus maximus*. (Rhode.)

In other Lumbricidæ the arrangement of muscle-cells inside a "case" is still more regular, since they surround the central hollow in a single layer, which gives a feathered appearance to the transverse section. The axis, which corresponds to the shaft of the feather, is bordered on either side by the oblique sections of the myoblasts, which cover the converging sides of each pair of cases (Fig. 6). In contrast with those, the longitudinal muscle-fibres of *Lumbricus olidus* and many Oligochetæ lie in a mass of irregular layers, or little groups divided by septa of connective tissue, as also occurs in Hirudinæ. The original epithelial character of the longitudinal muscles is thus no longer distinct in the arrangement of

the individual elements in such cases; but the structure of the single cells is otherwise perfectly conformable. A contractile, fibrillated, cortical layer can always be distinguished from a medullary substance (sarcoplasm), which it wholly or partially encloses. The usually solitary nucleus either lies to one side on the margin or surface of the separate fibres, or (e.g. in Hirudinæ) within the central protoplasmic hollow. In many Annulata, as in Cnidaria, the involution of the muscular lamella

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is excessively developed, and produces very complicated figures in transverse section. Certain Polychætæ, in particular, exhibit an extraordinarily complex arrangement of the flat band-like muscle-cells, which are individually of very insignificant proportions. The cross-section of the longitudinal muscle-layer not infrequently acquires a characteristic appearance.

The muscle-fibres of Cephalopoda should be mentioned as affording in many respects a remarkable instance of muscle-cells in Invertebrates. Their peculiar structure has recently been investigated by Ballo-witz (10).

With both the high and low power a system of parallel lines appears, running obliquely in opposite directions, and seeming with the medium power to cross directly over one another (Fig. 8). The examination of partially destroyed muscle-cells shows this to be the optical expression of fibres which "run in a continuous spiral in the cortex round the medullary substance."

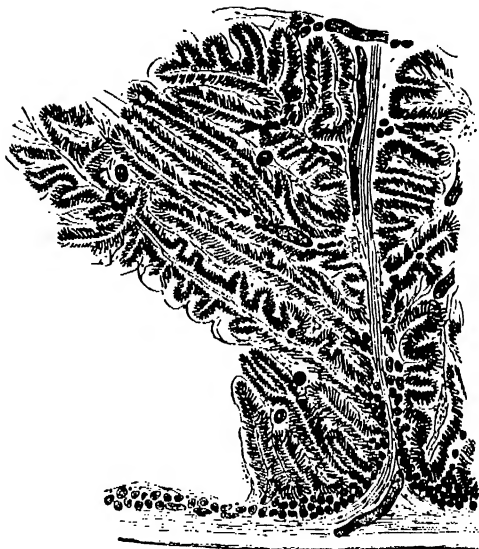


FIG. 7.—Transverse section of body-muscles of *Protula m* (Rhode.)

The steepness of the spirals varies considerably with the state of contraction. In very flat muscle-cells both systems of striation appear to lie almost in the same plane, giving an appearance of "double oblique striation," first described by Schwalbe (11) for several of the Invertebrates. Schwalbe explained these figures on the assumption that the fibres were composed of rhombic "sarcous elements," while Engelmann (12) at a later period pointed out their fibrillated structure, and maintained "that every fibre with double oblique striation consists of two systems of fibrils in concentric layers parallel to the surface of the fibre, which describe a spiral in opposite directions round its axis."

We further learn with regard to the finer structure of these muscle-cells, from transverse sections, that the proportion between cortical and medullary substance varies enormously in different elements of the same section. "The cortex may be small, and enclose a larger axial hollow, while other adjacent sections show a broad ring, with a narrow central lumen" (different states of contraction). In nearly all muscle-cells, especially in stained preparations of the cross-sections, it is possible to detect a radial striation of the cortical substance, similar in all respects to that

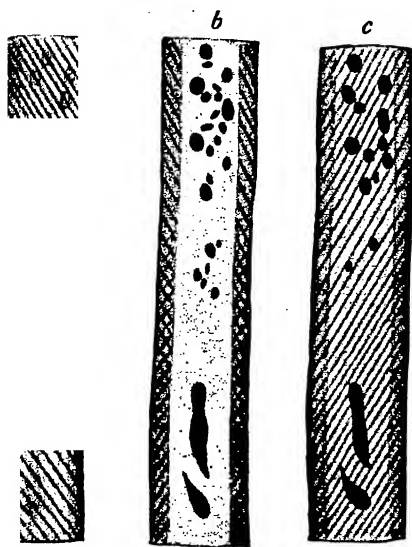


FIG. 8.—Segment of isolated muscle-cell from *Sepiola Rondeletti* under (a) high, (b) medium, and (c) low power. (Ballowitz.)

described above in the muscle-cells of Nematoda and Annulata, and therefore to be interpreted as the expression of a fibrillated structure (Fig. 9).

There is a regular alternation of dark and light striation, and it is easy to see that the dark lines correspond with cross-sections of the spiral fibres, which must accordingly be flat and band-like, while the colourless radii represent an intermediate substance. This appears, *inter alia*, from the fact that in focussing a thicker cross-section of a muscle-fibre "the dark lines all run out simul-

taneously in the same direction like the spokes of a wheel," when the tube of the microscope is gradually lowered. The spiral fibres of the cortex therefore form flat bands, which run in a single layer throughout its entire thickness. These spiral lamellæ obviously correspond with the radial "fibrillar laminæ" of the muscles described above, and exhibit a further differentiation into delicate homogeneous fibrils, the proper elements of the cortex. The reaction of these muscle-fibres to gold chloride is of great interest, especially in view of certain facts which we shall discuss later. Only the axial sarcoplasm is stained under some conditions, together with the interstitial substance that separates the spirals of the

lamella, and does not stain with any other reagent. The lamella itself remains colourless. This, as will presently appear, arises from a reaction common to all muscles—on the one hand, of the plasmatic ground-substance, on the other, of the contractile fibrils—which thus affords an invaluable means of studying the distribution of the two within one fibre. From this reaction we may conclude that the interfibrillar substance (which of course forms a spiral lamella) is identical with the axial sarcoplasm, so that the cortical substance in other cases also should contain formative plasma in addition to the contractile fibrils,—as is directly proved by the radial striation of the cross-sections. There is, however, a deplorable lack of any systematised comparative observations on the finer structure of invertebrate muscle according to modern methods.

Knoll (13), writing on the relative scarcity and abundance of protoplasm in muscle-fibres, communicated numerous data, which, however, bear less on the finer structure of the cortical substance than on the proportion between sarcoplasm and contractile substance in the muscles of vertebrate and invertebrate animals. From these, as well as from earlier researches (H. Fol, 14), it is evident that the muscle-cells of Lamellibranchs and Gasteropods have in many cases the same structure as those of Cephalopoda. The appearance of double oblique (in many cases also of transverse) striation in the muscle-cells of the adductor muscle of the Lamellibranchs is very interesting. Fol, previous to Ballowitz, had established an analogous theory of structural relations, since he described the contractile sheath of the spindle-cells as consisting of fibrils running spirally round the plasmatic axis. Like Ballowitz, he referred the figure of quadratic or rhombic area, first described by Schwalbe, simply to the crossing of the two halves of the spiral windings, running



FIG. 9.—Transverse section of muscle-cell from the mantle of *Eledone moschata*. (Ballowitz.)

above and below the axis. Rhode (*l.c.*) noticed the same appearance in the bi-obliquely striated muscle-cells of many worms (*Arenicola*, *Nephtys*). The bisected adductor muscle of Molluscs often shows, even to the naked eye, a division into two parts, distinct in colour and general appearance, the one white and tendon-like, the other glassy and transparent, of a grayish-yellow. The spindle-shaped muscle-cells of the former generally exhibit a well-marked longitudinal striation as the expression of fibrillated structure, while the more extended and flattened fibres of the gray part are often striped bi-obliquely (*Ostrea*, *Anodonta*, etc.), and in many cases they also show a definite transverse striation (*Lima*, *Pecten*). As we shall see later, these varieties of structure are closely allied to differences of function, and it may be concluded, at least for *Pecten* and *Lima*, that the quick, flapping movements made by these animals are served by the striated part of the adductor muscle, while the smooth fibres effect the sustained persistent closure. The relation between cross-striation of muscle-fibrils and rapidity of the movement engendered is already apparent in the epithelial muscles of Cnidaria, where, as we have stated, the comparatively swift, swimming movements of the Medusa are produced by striated fibrils. This also accounts for the almost universal cross-striation of muscle-cells in the heart and masticatory apparatus of Mollusca, which otherwise, in regard to the finer structure of single elements, follow closely the forms of muscle-cells described above. There are still the spindle-shaped, freely branched, plexiform fibre-cells, which, as seen especially in transverse section, are generally rich in axial sarcoplasm, wholly or partially surrounded by the small fibrillar cortical layer. The latter once more exhibits frequently a distinct radial striation in transverse section, representing a regular alternation of layers of fibrillated substance and sarcoplasm. Sometimes the fibrils (bundles of ?) surround the plasma bodies of the cell in a single row of dots (Fig. 10, *a*); in other cases the cortical layer seems to correspond with a continuous stratum of contractile substance.

Even a superficial comparison of cross-sections through the cardiac or masticatory muscles on the one hand, and the adductor, or pedal, muscle respectively on the other, in Lamellibranchs and Gasteropods, shows that the relative distribution of sarcoplasm, and of contractile fibrils separated out from it, varies very consider-

ably in the two cases. While in the cells of the adductor and pedal muscles the formative plasma is insignificant in comparison with the contractile substance, in the cardiac and masticatory muscles it preponderates. Knoll, who first investigated these differences systematically, used the terms *a-plasmic* ("clear") and *plasmic* ("dark") to designate the two cases, the cells of the cardiac and masticatory muscles being by far the richest in protoplasm, and less transparent. These comparative investigations prove beyond doubt that the structural ratio is, like cross-striation, of functional significance, as also appears from observations on the muscles of higher animals to be discussed below. The cardiac and buccal muscles have obviously more work, and more persistent work, to do than the adductor muscle of molluscs or the pedal muscle of snails, which are used less frequently, and since the formative plasma stands, as will be shown, in close relation with the nutrition of the contractile substance, we can readily appreciate the proportions given.

This theory is substantially confirmed by the "float" muscles of *Carinaria*. That portion of the foot which is used for floating, and is in constant movement, corresponds both in the cross-striation of the fibrils, and the abundance of its sarcoplasm, to the type of dark "plasmic" muscle-cells characteristic of the buccal and cardiac muscles of Mollusca. Along with the greater richness of sarcoplasm there is often a more or less definite *coloration* of the muscular elements. The cardiac and masti-

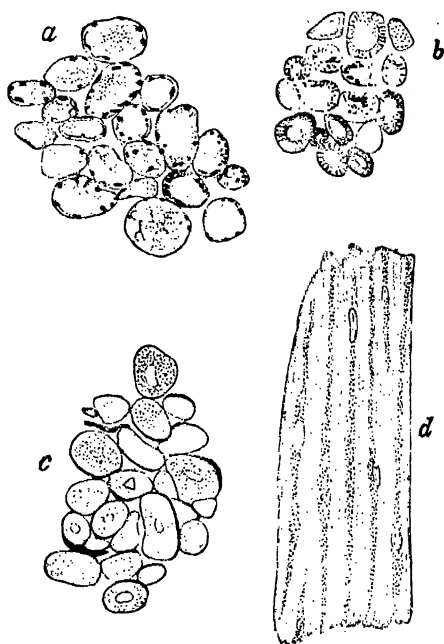


FIG. 10.—Transverse section of muscle-cells of Mollusca. (Knoll.) *a*, Heart of *Aphysia punctata*; *b*, heart of *Aphysia tinuicincta*; *c*, masticatory apparatus of *Carinaria*; *d*, longitudinal view of muscle-cells from buccal mass of *Aphysia punctata*.

catory muscles of many molluscs are yellow, pink, and even deep red.

Knoll discovered a remarkable instance of "plasmic" muscle-cells among Invertebrates, in the thin muscle-bands of the mantle of *Salpa* (*S. maxima*, *africana*, *pelesii*). The cross-striped, cylindrical fibres are very long, with conical ends. They are easily split up longitudinally into finer bundles and fibrils, owing to the

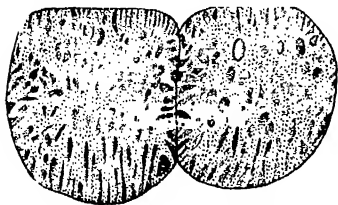


FIG. 11.—Transverse section of two muscle-cells from *Salpa pelesii*. (Knoll.)

excessive abundance of sarcoplasm, which intersects the plexus of fibrils, and as we see in transverse section, not only collects in the axis of each fibre, but also runs out in wide, radial tracts towards the periphery, thus dividing the contractile and distinctly fibrillated cortical stratum into separate laminae (Fig. 11).

The same plan of structure is here to some extent repeated on a larger scale, that prevails in the far more delicate radial striation of the cortical zone of muscle-cells in many worms and molluscs. But there is one important difference; the contractile substance is no longer (as in all previous cases) exclusively at the periphery of the formative cell, but appears in more or less conspicuous bundles (*muscle-columns*) within the central sarcoplasm also. Hence, as Knoll has pointed out, the *Salpa* muscles in a measure represent the transition to certain arthropod and vertebrate muscles, in which the same structural arrangement is present. A transverse section through the cardiac muscles of Crustacea often exhibits an unmistakable similarity to *Salpa* in disposition of sarcoplasm and contractile substance, except that the sarcoplasm is, where possible, even more richly developed, and all the "muscle-columns" lie within the formative cell (Fig. 12).



FIG. 12.—Transverse section of cardiac muscle-cell of Lobster. (Knoll.)

The unusual quantity of protoplasm is explained in both cases by the sustained and strenuous work which is served by these muscles.

From these observations we may conclude that there is no fundamental difference in structure between the different muscle-cells of Invertebrates (excepting only the muscular fibres of Arthropoda); whereas among Vertebrates we shall find striking

distinctions, morphological as well as physiological, between the several muscles—vegetative and animal. This is admitted, in a general sense, by the common division of vertebrate muscles into two chief groups—*smooth* and *striated*. The latter are technically opposed as muscle-*fibres*, in a strict sense, on account of their length, to muscle-*cells* with a single nucleus.

The smooth muscles and striated cardiac muscle-cells of Vertebrates are the natural continuation of the uninucleated muscle-cells, smooth and striated, of Invertebrates, inasmuch as they are mainly composed of short, usually uninuclear, elements of a more or less distinctly fibrillated structure, which, viewed from the surface, appear for the most part extended and spindle-shaped. As regards smooth muscle-cells in particular, they are not infrequently drawn out into fibres, without any consequent increase of nuclei.

In cross-section the contractile fibre-cells appear either rounded (when solitary), or flattened by the pressure of the tightly-crowded elements into a polygon or band-shaped figure. The long, oval, often "rod-like" nucleus always lies in the middle of the cell, surrounded by a somewhat richer accumulation of formative plasma. Wherever it is possible to recognise the fibrillated structure (and this is by no means invariable); the fibrils appear as a multitude of fine, smooth, cylindrical fibres, running parallel to the long axis of the cells, and—as seen in transverse section—bedded in a seemingly homogeneous mass of sarcoplasm (Fig. 13).

But while in nearly all the cases we have been considering (of Invertebrates) the fibrils occupied only one part of the section, surrounding the sarcoplasm in a ring or segment, in the smooth muscle of Vertebrates the fibrils are, as a rule, distributed equally over the entire surface. It is highly probable that fibrils must also exist in the cases where it has so far been impossible to detect them. Sometimes they are very obvious, and appear, *e.g.*, in the fibres of the frog's stomach—Engelmann (12)—in transverse section, with a high power, as little circular dots or spaces, which



FIG. 13.—Central part of isolated, smooth muscle-cell from Frog's stomach. (Engelmann.)

do not vanish on raising or lowering the objective. The number of fibrils in the section diminishes towards the end of each cell owing to their unequal length (Engelmann). The fibrils are so highly refractive that it is sometimes difficult to recognise the boundaries of adjacent cells, and a muscular layer of the kind we are describing may even appear as a single, undifferentiated mass of fibrils.

Smooth muscle-fibres do not, for the most part, occur singly, but arrange themselves into bundles, membranes, or bulky masses. The finer and more delicate bundles of muscle-cells are often united into a net with wide or narrow meshes, each adjacent process anastomosing with its neighbour by branches. The bladder of amphibia is a fine illustration of such a net with wide meshes. Among Invertebrates a similar plexus of uninuclear muscle-cells is found in the heart of molluscs, sucker of echinoderms, etc.

The intestine of Vertebrates is the best example of the structure of a membrane composed of smooth muscle-cells. Here the arrangement of fibre-cells in two layers, crossing at right angles, which is characteristic of most hollow organs whose walls contain smooth muscle-fibres, is very conspicuous. A similar arrangement, *i.e.* a longitudinal and a circular muscle-layer, within which the axis of the fibres stand vertically to each other, is found in the ureter, and among Invertebrates in the cutaneous muscular layer of worms.

The anatomical relations of adjacent muscle-cells with one another is a point of great interest. A number of physiological facts pointed to direct conductivity from cell to cell, in certain smooth muscles, long before histology gave substantial support to the conjecture. The idea of a direct communication by means of protoplasmic bridges between adjacent cell-elements (which is not at all a new hypothesis) has recently obtained extensive confirmation on the botanical side, and in animal histology such cell-bridges have long been known in particular objects (bristle or prickle cells of the epithelium). Analogous structures have recently been described in smooth muscle-cells also. In the transverse section of a crowded tract the single elements appear to be united by a homogeneous cement substance, which gives a reaction similar to that of the cement substance of endothelium. With certain very preservative hardening methods, it becomes possible to see under the high power, that the single cells in the transverse

direction are connected by fine protoplasmic bridges, between which are small intercellular spaces (Fig. 14).

Common as is a marked pigmentation in the uninuclear, invertebrate muscles, it is but seldom that we find definite coloration of the smooth muscle-cells of vertebrates. The bright red muscles of the gizzard of many birds are, however, an exception, as well as the contractile *fibre-cells*, crowded with dark-brown pigment granules, in the iris of many fishes and amphibia, which, according to Steinach (15), owe to these their direct excitability to light.

We must not omit to mention certain very peculiar figures obtained from smooth muscle-fibres that have been fixed during contraction. A highly regular transverse striation is often visible, due presumably to swelling from the contractions that follow one another at regular intervals. The figures were first pointed out by Heidenhain in 1861 (16), and Drasche has recently supplemented our imperfect knowledge of them (17). He observed a regular cross-striation in the individual fibre-cells of the contracted muscular coat of the poison-gland of Salamander, resulting from a delicate transverse grooving, or marked involution, produced by the contraction of the lower surface of the muscle. Similar very delicate figures were observed in the muscle-cells of a cat's intestine that had been hardened in alcohol (Biedermann). The sharply defined, highly refractive, transverse swellings gave an impression of local (fixed) waves of contraction, such as occur occasionally in certain striped muscles.

Apart from the Arthropoda, in which uninuclear muscle-cells seem to be altogether wanting, the existence of *true* cross-striation, *i.e.* disposition of each single fibril in layers of different optical relations, would appear from the foregoing to be comparatively rare in muscle-cells; its physiological significance has already been indicated.

The much commoner oblique striation stands, as we have said, in no sort of relation to the transverse striæ, since the single fibrils are not further differentiated, and deviate in direction only from the normal. We find it impossible to subscribe to the theory recently advanced by Knoll to the effect that there is no sharp



FIG. 14.—Transverse section of the bladder-muscles of Rat (cell-bridges). (From C. de Bruyne, *Arch. de Biol.*, van Beneden, vol. xii, 1892.)

distinction between oblique striation and cross-striation proper, so that one and the same cell may present oblique or transverse striæ under different conditions. It seems more probable that the effect is due partly to different states of contraction in adjacent fibrils, partly to a longitudinal displacement (transposition) of the fibrils.

In Vertebrates also, in the adult state, it is exceptional to find transversely striated uni- or binuclear muscle-cells; they occur in cardiac muscle, and in a peculiar development of the endocardium of ruminants, horses, pigs, and other mammals, and in certain birds. As a rule, the elements of cardiac muscle

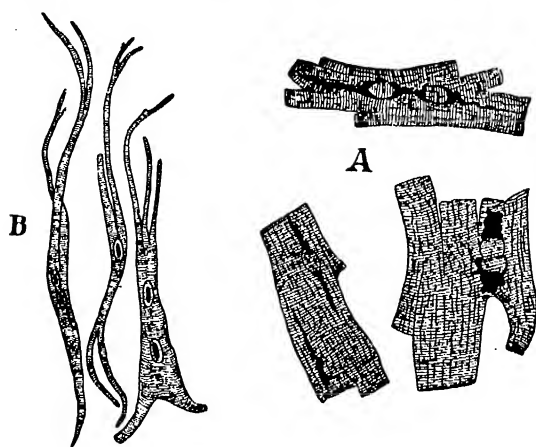


FIG. 15.—Isolated cells of cardiac muscle. *A*, from Man; *B*, from *Rana temporaria*. (Schiefferdecker.)

either resemble the smooth, spindle-shaped fibre-cells (fishes, amphibia), though they exhibit many irregularities of processes and branches, or form somewhat irregular cylindrical or flattened cell-bodies, anastomosing at the ends with the adjacent elements in a network of branches

by means of short broad processes, of which the smooth superficies are closely applied together (mammals, birds, reptiles) (Fig. 15). In many cases the component cells are still clearly visible; in others they have disappeared, or become hard to recognise.

These principal types of cardiac muscle are connected by many transitional forms. As so often in the elements of smooth muscle, the cardiac muscle-cells form *inter se* a physiological as well as an anatomical continuum, being, like many epithelia and endothelia, united by a cement substance, which stains black with AgNO_3 , and through which transmission of the excitatory process is apparently effected. Whether there is here the same anastomosis of adjacent cell-bodies by bridges of protoplasm as in many smooth muscles, has not been determined.

The arrangement of the cross-striated fibrils within the formative plasma (sarcoplasm) is very remarkable. The sarcoplasm is so abundant both in vertebrate and invertebrate animals, that the otherwise non-membranous cardiac muscle-cells come under the category of "dark" muscles, with which their easy separation into fibrils and bundles of fibrils also coincides. In transverse section the cardiac muscle-cells of Fishes and Amphibia exactly carry on the type of Cephalopods and Gastropoda, each spindle-cell exhibiting a richly developed, central, medullary substance surrounding the nucleus, and enclosed in its turn by the transversely striated fibrils of the cortical substance, which are often arranged in radial strata.

The heart of Reptiles and Birds is characterised by the same structure; the contractile cortex of the latter in particular frequently exhibits distinct radial striation. In Mammals also the elements of the cardiac muscle (which is here, as in other vertebrates, of a deep red colour) are among the most richly protoplasmic parts of the body. The distribution of sarcoplasm and fibrils closely resembles the spindle-cells of *Salpa* described above; the bundles of fibrils (Kölliker's "muscle-columns") not only form a peripheral cortical zone, but are developed within the central nucleated axial plasma (Fig. 16). The plasma itself is usually accumulated round the nucleus, which lies somewhat toward the centre of each cell. The bundles of fibrils (muscle-columns) present considerable variations of form and arrangement in different mammals. The radial, band-shaped bundles of fibrils, striped in cross-section, with which we are so familiar in Invertebrates, and also in certain muscles of the lower Vertebrata, but which appear only in the heart of Mammals (dog, porpoise), are very frequent. Often, besides these band-shaped muscle-columns, which figure in transverse section as a radially striated, laminar, cortical zone, another prismatic section—rounded or polygonal—appears in the centre of the muscle-cell (dog, man) (Fig. 16). And, in conclusion, there are many examples (pig) in which these last only are present.

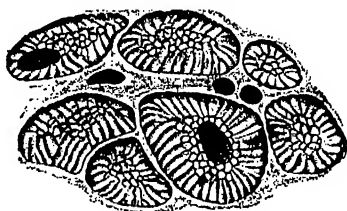


FIG. 16.—Transverse section of cardiac muscle-cells—Man. (Kölliker.)

Generally speaking, therefore, it may be said that, in regard to histological structure, the cardiac muscles exhibit great similarity with certain muscles of the lower animals and the developing stages of cross-striated, multinuclear muscle-fibres, and are thus in a certain sense embryonic in character. This applies not merely to the striking abundance of sarcoplasm, but also to the form and arrangement of the muscle-columns, and central situation of the nucleus.

The elements of cardiac muscle in Vertebrates, in particular of mammals, together with the cross-striated uninuclear cells of Invertebrates, form the transition to the type of muscle which is, anatomically and physiologically, the most highly developed.

CROSS-STRIATED, MULTINUCLEAR MUSCLE-FIBRES

Among Invertebrates these occur in Arthropoda only; in Vertebrates, collectively, they form the chief bulk of muscle.

At one time it was supposed, chiefly on account of the multiplicity of nuclei in striped muscle-fibres, that these represented a fused series of many cells (a "syncytium"), but it is now admitted that *each striated muscle-fibre is equivalent to a single cell*, from which, indeed, it has developed. At first these are uninuclear, spindle-shaped cells, which grow rapidly longer, while the nucleus increases by repeated division. Subsequently the elongated, multinuclear spindles become not only longer, but much wider, while a gradual differentiation of striated fibrils is proceeding from the increasing bulk of protoplasm (sarcoplasm). These fibrils, viewed longitudinally, or better in transverse section, do not occupy the entire thickness of the fibre, but arrange themselves superficially as a tubular sheath, or (in many of the lower vertebrates) as a segment lying to one side, so that the nucleated, formative (sarco-) plasma lies, as it were, enclosed in a canal or furrow (Fig. 17).

A *temporary* relation thus arises between the latter and the differentiated fibrils, which is altogether analogous to the constant distribution of the permanently uninuclear myoblasts of most invertebrates. As development progresses the peripheral layer of fibrils, at first extremely attenuated, increases in bulk at the expense of the sarcoplasm, so that eventually the ratio is

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reversed; the fibrils form the chief bulk of the fully-developed muscle-fibre, while the remains of the formative plasma, together with many nuclei, is interspersed between the mass of fibrils, in varying bulk and disposition. Each fibre thus presents a long, cylindrical, prismatic figure, with conical or blunted ends. The fibres are usually undivided, but may branch more or less freely with many nuclei, and even form an anastomosis.

The multinuclear, striated muscle-fibres must be reckoned among the largest cells with which we are acquainted. According to Kölliker the uninuclear, spindle-shaped myoblasts of the human embryo, seven to eight weeks old, are already 132 to 176 μ in length, and over 300 μ a little later.

In adult muscle-fibres, Felix finds some that certainly exceed 12 cm. in length, to which we must add that the fibres, even thus, were not at their greatest extension. The bulk is relatively very small; it is greatest at an early stage of development. According to Felix human muscle-fibres at the third month attain the considerable diameter of 13 to 19 μ ; these dimensions are rare in older embryos, and only re-appear in the new-born infant.

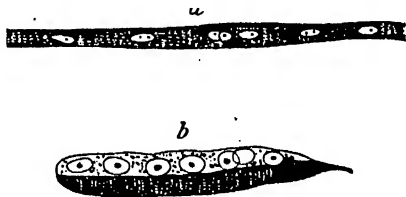


FIG. 17.—Embryonic muscle-fibres. *a*, Man; *b*, Frog. (Kölliker.)

The length of the single primitive fibril is in no regular ratio with the length of the muscle developed from it. Whereas formerly it was supposed that the muscle-fibres, generally speaking, corresponded in length with the coarser muscle-bundles, it is now known that numerous fibres, particularly in the longer muscles, terminate freely, are shorter, *i.e.*, than the whole muscle. Both free ends accordingly may be pointed, and the whole fibre spindle-shaped, or one end only may be free, and the other blunt and connected with the tendon. In small muscles, on the contrary, according to Kölliker, all the fibres run the length of the entire muscle, and are generally rounded off at both ends.

Nearly all cross-striated, uninuclear muscle-fibres (excepting only in certain Arthropoda) possess a distinct sheath, the sarcolemma, which consists of a fine, transparent, structureless membrane, lying next to, and closely investing the contents of,

the primitive bundle (sarcoplasm with nuclei and fibrils); it can, therefore, only be seen clearly in places where, from rupture of the fibres, or any other cause, the contents of the muscular sheath have shrunk back from the wall, or where, conversely, the latter has risen up in a bladder (imbibition of water). The sarcolemma, which Kölliker reckons in vertebrates as a true cell-membrane, may be seen even at an early stage of development in the muscle-fibres as a very delicate integument; other authors regard it as a product of the connective tissue that surrounds the muscle-cell.

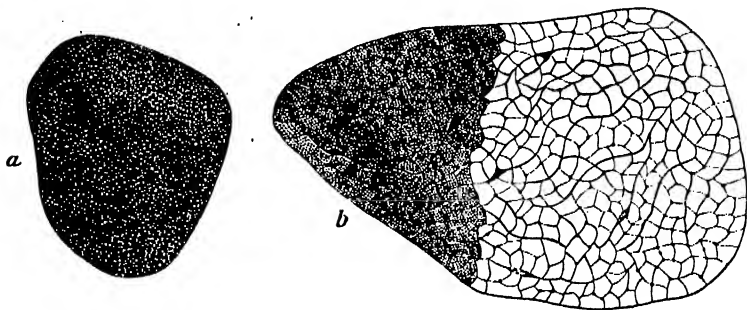
In accordance with the usual disposition, multinuclear muscle-fibres severally exhibit more or less distinct transverse striæ, at right angles, *i.e.*, to the axis of the fibre, a characteristic common also to many uninuclear muscle-cells of invertebrates and vertebrates, and due, as will be shown, to the same cause in both instances.

In addition to the transverse striæ, a *longitudinal striation* (derived from the fibrillated structure) is nearly always apparent; it may be excessively fine, or may separate the fibres into comparatively large bundles.

The relative distinctness of the transverse and longitudinal striæ at a given moment varies very considerably in different muscle-fibres. In many cases the cross-striation is hardly visible, while the longitudinal striæ are clearly marked; at other times the opposite appears. Different parts, indeed, of one and the same fibre may vary in this particular. This is essentially dependent upon the *relation between the contractile fibrils and the interfibrillar sarcoplasm*, which (as many recent observations have established) may vary enormously, alike in the muscles of different animals, and in the different muscles of the same species. As was stated above, the examination of cross-sections gives the best and surest conclusions. The salient feature under all conditions is, in the fully-developed fibre also, the unequal distribution over the surface of the section. The fibrils are arranged in larger or smaller *bundles* ("muscle-columns"), separated by more or less bulky discs (striæ, from the longitudinal aspect) of sarcoplasm (*interstitial substance, interfibrillar substance, sarcogleia*), as in so many smooth and cross-striated uninuclear muscle-cells. The more abundant the sarcoplasm, the easier the division of a primitive bundle into "muscle-columns," *i.e. bundles of*

which by proper methods can again be split up into the true elementary fibrils. As in the uninuclear muscle-cells, the multinuclear muscle-fibres fall in the main into two distinct forms or types of "muscle-columns." These are either, as in many invertebrate muscles, flat band-like bundles, composed of a single row, or some few rows, of fibrils only, or (as is more common) the bundles appear to be cylindrical or prism-shaped, *i.e.* circular or polygonal in cross-section.

When, as in the majority of cases, the prismatic "muscle-columns" are separated by a comparatively insignificant mass of "interstitial substance," a mosaic of polygonal areas appears in transverse section—as first described by Cohnheim; whence, therefore, the name of *Cohnheim's Areae* (Fig. 18, *a*, *b*).



18.—*a*, Transverse section of muscle-fibre of Rabbit (bundles of fibrils dark, sarcoplasm clear). (Kölliker.) *b*, Transverse section of muscle-fibre of Frog, showing on the left cross-sections of the fibrils. (Schlefferdecker.)

It is questionable whether the sarcoplasm that surrounds the muscle-columns penetrates also between the individual fibrils: Rollett disputes it; Kölliker assumes a minute amount of interstitial matter, identical with the sarcoplasm—it can only be identified under a very high power, and forms an investing sheath along the entire length of each fibril.

From this last point of view each muscle-fibre must be regarded as a bundle of fibrils which are held together by an uneven accumulation of intermediary substance. "According as this accumulation is more or less abundant, the muscle-columns are more or less well defined, larger or smaller" (Kölliker).

The comparative proportion of the two chief constituents of a muscle-fibre, *i.e.* the fibrils (Kühne's *rhabdia*) and the sarcoplasm, varies, as we have said, in different animals, and in different

muscles of the same animal; and the same is true of the position of the nucleus. Two groups of striated fibres can again be distinguished in vertebrates, *i.e.* those which have much, and those which have little, sarcoplasm. The fibres of the first group, generally, look rather dark when examined with the microscope,

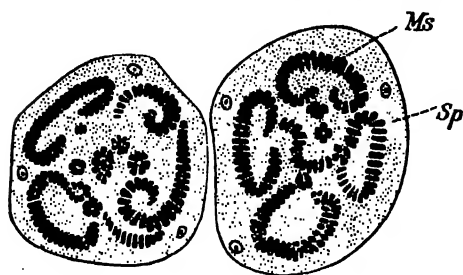


FIG. 19.—Transverse section of two float-muscles of *Hippocampus*. (*Ms*), Bundles of fibrils (muscle-columns); (*Sp*), sarcoplasm. (Rollett.)

owing to the large number of interstitial “granules” with which the sarcoplasm is studded; the cross-striæ are indistinct, the longitudinal well marked. The a-plasmic fibres, on the other hand, are clearer and transparent, with sharp transverse striæ.

In the same sense, we have already, in describing the structure of the uni-nuclear muscle-cells of invertebrates and vertebrates, had occasion to distinguish between clear and dark, plasmic and a-plasmic elements; cardiac muscle-cells in particular being universally dark and plasmic. The float muscles of the Seahorse (*Hippocampus*) exhibit a peculiarly typical example of plasmic, multinuclear muscle-fibres in the Vertebrates. In transverse section the flat bands of muscle-fibrils (muscle-columns) are seen, as in the muscles of *Salpa*, or the cardiac muscle of Crustacea (*supra*), forming irregular groups and columns in the sarcoplasm, which is here excessively abundant, and presents a thick cortical layer in which the nuclei are embedded (Fig. 19). Similar bands of muscle-columns are found in the lateral muscles of the carp, which are also characterised by an abundance of nucleated sarcoplasm lying close under the sarcolemma (Fig. 20).

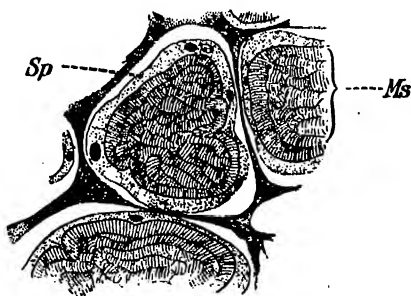


FIG. 20.—Transverse section of lateral muscle-fibres of Carp. (Kölliker.)

Other muscle-fibres (lateral trunk-muscles) in the same fish—

like many cardiac muscle-cells (man, horse)—show a peripheral layer of the flat bands of fibrils, while the interior is filled with polygonal bundles. The nuclei are again embedded in the layer of sarcoplasm that surrounds the entire fibre. A corresponding structure is found in the same muscles of other fishes.

In the higher vertebrates, a transverse section of the skeletal muscle usually exhibits polygonal areas, separated by a very small quantity of sarcoplasm (*Cohnheim's Area*, Fig. 18, *a*). But there

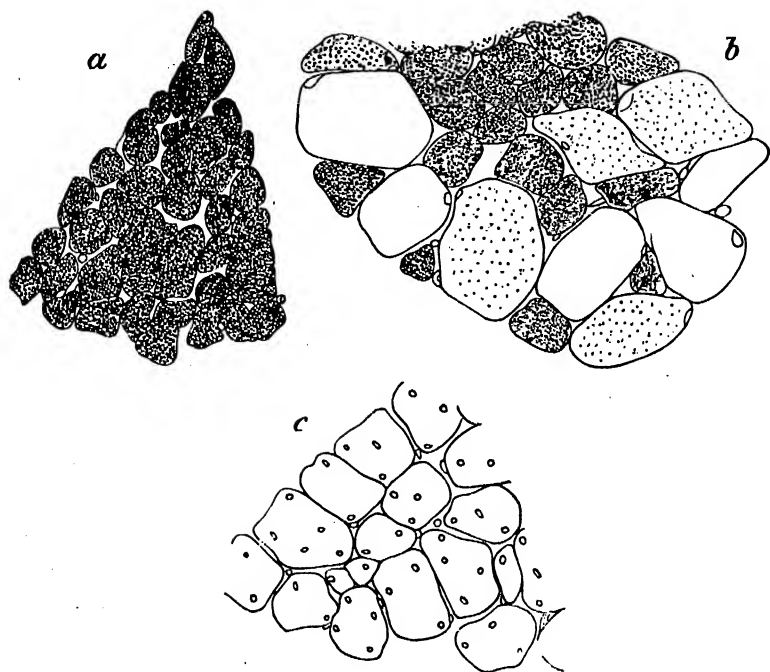


FIG. 21.—*a*, Transverse section of *Pectoralis major* in Falcon; *b*, *ib.* Goose; *c*, *ib.* Hen. (Knoll.)

are still distinctions corresponding with dark and clear muscles, greater or less abundance of sarcoplasm. In Amphibia the clear fibres usually predominate; the throat muscles of batrachians are, however, an exception. Knoll also found a considerable development of sarcoplasm in the jaw muscles of reptiles, and the limb muscles of *Lacerta* and *Cistudo*. In birds, on the other hand, the dark, plasmic fibres prevail, and constitute the pectoral muscles used in flight. In the hen the muscles of the breast and back consist, however, exclusively of light fibres, which are

again in a minority in the same parts of the goose and pigeon, while they are wholly wanting in the falcon, crow, and sparrow (Fig. 21).

From birds onwards the dark fibres are usually in the ascendant. According to Rollett the elements of the skeletal muscles of the bat are peculiarly rich in sarcoplasm. In transverse section it appears as a number of coarse, irregular knots, drawn to one side or the other, and united by fine, slender bridges of protoplasm; the muscle-columns lie in the intermediate spaces (Fig. 22, *a*).

The superficial aspect of the fibres is correspondingly coarse,

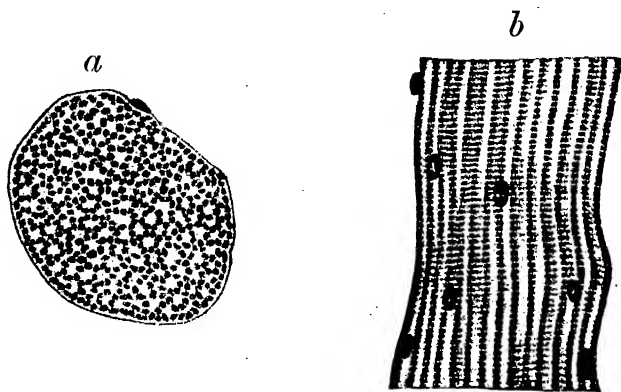


FIG. 22.—Transverse and longitudinal sections of the muscle-fibre of Bat. Sarcoplasm clear, fibril-bundles (muscle-columns) dark. (Rollett.)

with longitudinal striæ, due to the alternation of sarcoplasm and muscle-columns (Fig. 22, *b*). In most other mammals the dark and relatively plasmic fibres are intermixed with clear fibres in the skeletal muscles. Knoll finds that the optic, masticatory, and respiratory muscles (in particular the diaphragm) are specially rich in dark fibres. In almost all vertebrates the dark are smaller than the clear fibres. This is well shown in transverse sections of muscles containing both kinds of fibres (pectoral muscle of pigeon, most muscles of amphibia and mammals) (Fig. 21). Moreover, the "dark" fibres in many cases are characterised by their deep red colour, while the "clear" fibres are paler. The dark lateral muscles of many fish, *eg.*, and the float and cardiac muscles, are intensely red; in *Rana escul.* and *temp.* also, the muscles of the throat and heart are dark and red.

The striated muscles of mammals are mostly red, and (with the exception of the cardiac muscle-cells, and the muscles of the bat, which are uniformly dark) contain a mixture of clear and dark fibres.

The variations of colour in different muscles are particularly striking in the domestic animals. Every one knows the "white meat" of breast and back in the common fowl, which consists exclusively of clear fibres, while the leg-muscles are red and dark in colour. In tame rabbits and guinea-pigs also, white pale muscles occur along with the strictly red of the heart, diaphragm, etc.; and here again dark fibres preponderate in the one case, and clear in the other, but the degree of colour and quantity of protoplasm are not always proportional. Thus in the pigeon the red wing-muscles are composed chiefly of dark, the equally red leg-muscles of clear fibres, and in the rabbit also there is little difference in amount of protoplasm between the dark red soleus and the pale adductor magnus muscles. In Triton and Salamandra, the leg-muscles are reddish, but distinctly dark in single fibres only; the rest of the muscles are pale and clear. Ranvier also finds a distinction in number and distribution of the nuclei between red and pale muscles, but, according to Knoll, no general rule can be laid down. In all mammalian muscles investigated by him, the nuclei are "predominantly" set round the periphery of the fibre, but there are always individual fibres with instanding nuclei, and this not only in the red muscles as stated by Ranvier, but in the definitely pale muscles also (adductor magnus of rabbit). Generally speaking, the centrally-situated nucleus corresponds with a low grade of development in muscle-fibre, and is therefore the rule only in fishes and amphibia, in which last many nuclei are often strung together in a longitudinal series, while in the muscle-fibres of birds and mammals the nuclei are generally placed at the periphery, close under the sarcolemma; but here again there may be exceptions.

Within the sarcoplasm, which, as follows from its development, represents the original formative plasma, lie the structures described by Kölliker as "interstitial granules," and these, in virtue of their strong refractibility, are, when accumulated between the bundles of fibrils, the cause of the "dark," opaque properties of certain muscle-fibres.

The greatest variety of mass-disposition, and relative proportion of sarcoplasm and fibrils, is exhibited by the *striated muscle-*

fibres of the Arthropoda, which, anatomically and functionally, have reached the highest development. In view of certain important differences of structure, that must correspond with no less

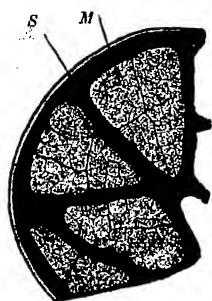


FIG. 23.—Transverse section of muscle-fibre, *Maja Squinado*. S, sarcoplasm. M, muscle-column.

(Schiefferdecker.)

significant differences in function, two main types of striated fibres may be distinguished, which, although they exist only in certain of the Arthropoda, are always differently localised. These are what Kölliker has termed “*typical*” and “*a-typical*” fibres; the first presenting essentially the same organisation as the fibres of vertebrates, while the second, which exist only in the thoracic muscles of winged insects, are very divergent in structure. With regard to the first type, we may distinguish, as in vertebrates, fibres with prismatic columns (polygonal in transverse section), and fibres with flat bands of fibril bundles. The muscles of Crustacea (*Astacus*) are a typical example of the first, exhibiting in cross-section just such a mosaic of polygonal Cohnheim’s areas as we find in most vertebrate muscle-fibres (Fig. 18, *b*). The sarcoplasm, however, is always more abundant;

it separates not merely single muscle-columns but whole groups of them, forming (as in the muscles of Amphibia) thick and usually nucleated lamellæ in the interior of the muscle: the sarcoplasm also forms a continuous sheet, greater or less in thickness, immediately beneath the sarcolemma (as in certain muscle-fibres of fishes).

The muscles of *Maja Squinado* (Fig. 23) afford another elegant illustration of this structure of fibre. In Beetles the polygonal prismatic muscle-columns are very prominent; the sarcoplasm lies evenly distributed, or is unequally heaped up in parts of the transverse section.

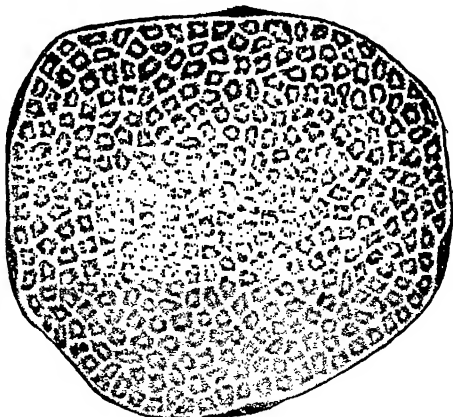


FIG. 24.—Transverse section of muscle-fibre, *Hydrophilus*. Sarcoplasm clear, muscle-columns dark. (Rollett.)

Sometimes the sarcoplasm will be found only in the centre of the fibre, densely heaped up in a round, or slit-like, cavity. The muscle-columns, which in such cases form broad bands, are set radially round the central mass of nucleated protoplasm, like the leaves of a book, separated only by very fine lamellæ of sarcoplasm, a disposition already familiar to us in the uni-nuclear muscle-cells of many invertebrates. According to Rollett, the direct transition to this most characteristic structure in the muscles of the Dytiscidæ is found in numerous little Carabidæ, *e.g.* Brachinus, and the common wasp, where the muscle-fibres are more or less elongated in cross-section, and present radially situated Cohnheim's areæ in their longer diameter.

Retzius (19) was the first to describe the very delicate transverse figures exhibited by the muscle-fibres of *Dytiscus marg.* in

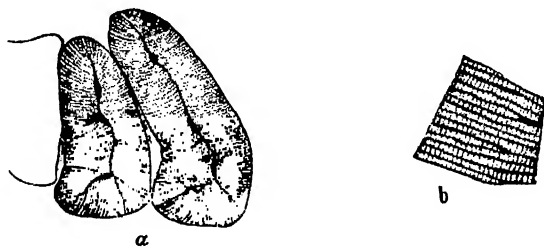


FIG. 25.—*a*, Transverse section of muscle-fibres (extremities) of *Dytiscus marginatus*; *b*, part of the section on application of dilute acids. Small secondary strata denoting the cross-sections of single fibrils appear between the primary strata of sarcoplasm. (v. Limbeck.)

gold chloride preparations, to which we shall return presently (Fig. 25). But his interpretation of the figures (adopted later by Bremer, v. Gehuchten, and Ramon y Cajal) must be regarded as fallacious, chiefly on the ground of the classical researches of Rollett. Retzius conceived the central muscle-nuclei with the surrounding sarcoplasm to be true cells (analogous to Schultze's *muscle-corpuscles*) with excessively fine processes, and believed that these filiform nets, stretched horizontally in the muscle-fibre, were arranged at regular intervals one beyond the other, the fibrils lying in their meshes. On this assumption, the outlines of Cohnheim's areæ, whatever their individual shape, must be viewed not as the optical expression of the sarcoplasm accumulated at the edges of the muscle-columns, forming a network of partitions right along the muscle-fibres, but as the superficial aspect of the

superposed nets of filaments, consisting of the cell processes of the muscle-corpuscles, and only connected longitudinally by fine, small fibres. Apart, however, from the fact that the appearance of a muscle-fibre in optical transverse section must then vary with alterations of the objective, according as the cross-section of a fibre-plexus, or the space between two such, is focussed (when in the first case Cohnheim's area, in the second a mere system of dots, corresponding with the cross-sections of the connecting longitudinal fibres, would appear—which never is the case), the comparative study of the development and structure of fully developed muscle-fibres and cells of different animals appears to us to be conclusive evidence against this theory. For the rest, it is sufficient to

quote the masterly criticisms of Rollett (20).

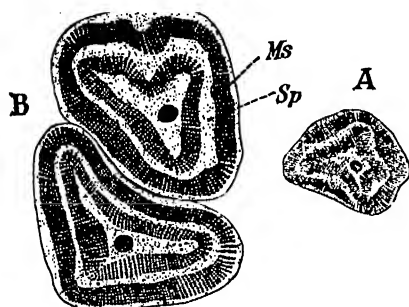


FIG. 26.—Transverse section of striated muscle-fibres of *Musca domestica*. A, Low power; B, highly magnified; Ms, bands of muscle-columns (bundles of fibrils); Sp, sarcoplasm. (Schleffer-decker.)

The muscles of Flies exhibit very peculiar structural relations (Fig. 26). In transverse section the bundles of fibrils are once more flat and band-like, and usually consist of a single layer of fibrils only. These, however, are so disposed in series that two or even three tubes are formed, fitting into one another, and separated by

strata of protoplasm, with which they are also filled and surrounded. The nuclei lie in the innermost, axial, plasma cylinder, as appears in the longitudinal section of such a fibre. These few examples will give an approximate idea of the multiplicity of figures in cross-section in the "typical" arthropod muscles. Before we pass on to the structure of the "atypical" wing-muscles (thoracic fibrils) of insects, the question as to the composition of "muscle-columns" out of "fibrils" must detain us for a few moments. In Insect as in Vertebrate muscles, the direct proof is harder to find than in many muscles of the Invertebrates. Even under the most favourable conditions, e.g. after treatment with gold chloride, which stains the sarcoplasm deep red or black, while the fibrillar substance remains uncoloured, so that each area of Cohnheim stands out distinctly, no further differentiation is

visible as a rule within the latter, even with the most powerful enlargement; the *areæ* appear to be perfectly homogeneous. By the use of proper means (alcohol, acid), which facilitate the breaking down of muscle-fibres into fibrils, or the swelling of the latter, it becomes, however, possible to detect the fibrils in cross-section. Cohnheim's *areæ* then appear to be subdivided into smaller fields lying in close juxtaposition (Figs. 25, *b*; 26, *B*). In longitudinal section also, the fibrillated structure of the muscle-columns—at least in places—becomes distinctly visible. Still it must be admitted that in comparison with the certainty with which the muscle-columns themselves can be demonstrated, their composition as *bundles of fibrils* is much harder to determine.

If the *typical* muscles of Arthropods already exhibit a superabundance of sarcoplasm in comparison with the majority of vertebrate skeletal muscles, this is to a far greater extent the case with the *a-typical* thorax muscles of Insects. As compared with the first type, these must be designated "dark" muscles, which is the more legitimate, since, like the "plasmic" muscle-cells and fibres of vertebrates and many invertebrates, they are generally distinguished by their darker colour (reddish, or brownish-yellow) from the clear, white leg-muscles. But the most typical characteristic of these wing-muscles (thoracic fibrils) of insects (discovered by Siebold, and first described minutely by Kölliker) is their readiness to separate into very broad fibrils (1 to 4 μ), which are bedded in the cavities of the copiously-developed sarcoplasm. The sarcoplasm again is richly studded with "interstitial granules"—which are often excessively large—and arranged in regular longitudinal series between the fibrils.

Further, on examining fresh preparations, the wealth of tracheæ is very striking. They not only wind themselves round the bundles of fibrils externally, but, as appears unmistakably in transverse section, penetrate *inside* the individual fibres, and ramify freely in the sarcoplasm. Within the meshes of the network of tracheæ, it is easy in cross-section to distinguish a mosaic of circles, corresponding with the single fibrils, whose diameter, as compared with the excessively fine, elementary fibrils of the leg-muscles, is enormous.

As a rule there is no sarcolemma in these larger bundles of fibrils (corresponding to *muscle-fibres*) in the wing-muscles of

insects; they are bounded only by the surrounding, spongy, connecting-substance, and supported inside by the system of branched tracheæ. The tracheal branches thus form, as it were, the skeleton of a fibril-bundle, while the sarcoplasm fills up the cavities that remain between fibrils and tracheal ramifications.

Glancing back over the facts that relate to mass-disposition of sarcoplasm, *vs.* contractile substance proper of the fibrils, the general conclusion seems to be justified, that *the elements of those muscles which serve the most persistent or most strenuous action are richest in sarcoplasm.* (Cardiac and masticatory muscles of invertebrates and vertebrates, float-muscles of Hippocampus and other fishes, some of the lateral body-muscles of fishes, especially those in the tail-region, which govern the movements of direction.)

Knoll (13, p. 47) pointed out, in this connection, a curious instance of divergence in the tail-muscles of Torpedo and Raja. In the former there is a well-developed stripe of red, dark muscle, which is totally absent in Raja; there are corresponding differences in the swimming movements of the two animals, since in Torpedo the flexible tail executes a series of rapid sideway movements, which do not occur with Raja.

The wing-muscles of birds and insects afford another example. The great pectoral muscle of the best fliers consists exclusively, or almost exclusively, of plasmic, in the weak-winged "fowls" predominantly of a-plasmic, fibres. In the guiding muscles of amphibia, reptiles, and mammals the a-plasmic and plasmic fibres are intermingled; the last are more abundant in the free, wild species of mammals than in the domesticated animals. In the rodents, *e.g.* (rabbit), they are entirely absent, or very sparsely distributed, in certain sections of the leg-muscles. In bats, on the other hand, the fibres of every muscle are rich in protoplasm.

There seems therefore to be *a direct relation between the extension and force of the contractile fibrils and the bulk of surrounding sarcoplasm* (Knoll).

If, as Sachs conjectured, the nutrition and metabolism of the muscle-fibrils (*i.e.* of the contractile substance) are intrinsically dependent on the bulk of sarcoplasm, this relation is easy to understand. As a matter of fact there can be no doubt that energetic chemical changes do go on in the sarcoplasm, as is

proved, *inter alia*, by the frequent appearance of fat-drops, which are presumably in close, genetic relation with the interstitial granules mentioned above (Knoll). Again, we know that certain matters which penetrate the muscle-fibres are further distributed to the sarcoplasm; *e.g.* Leo Gerlach (21) found that the muscle-fibres of frogs which had been treated for several days with indigo-carmin became speckled with blue, particularly towards the tendon end of the fibres, in consequence of the indigo assimilated, and often exhibited a definite, serial arrangement of the pigment. The rows of blue granules lie, like the fat-drops in other cases, between the fibrils in the sarcoplasm; so that the indigo-carmin must be taken up by the sarcoplasm in solution. If, then, it really is the *rôle* of the interfibrillar plasma to preside over the nutrition of the contractile substance, the greater abundance of sarcoplasm in the muscles which serve the most strenuous and persistent functions is readily intelligible. The frequent pigmentation of the dark, "plasmic" muscle-fibres (as previously cited) seems also to be closely related. Such are—in opposition to the body-muscles—the deep purple-red buccal muscles of many snails (*Chiton*, *Haliotis*, *Limnæus*, *Trochus*, *Paludina*, *Littorina*, *Patella*), the cardiac muscles of many invertebrates and all vertebrates, as well as the dark-red muscles which contain hæmoglobin.

The *finer structure of the single muscle-fibrils (infra)*, on the other hand, seems to be in relation with quite another property of the muscular elements, *i.e. rapidity of contraction*. We have already stated that distinct cross-striation of the fibrils is exceptional in the uninuclear cells of Invertebrates, and where it does appear (*e.g.* in *Medusæ*, adductor muscle of *Pecten*, etc.) exists only in the more swiftly contracting muscles. Thus O. and R. Hertwig (22) observed that the individuals of the Hydroid-colony have smooth muscle-fibres, so long as they remain attached as inert hydroid polyps to the parent, "but acquire striated fibrils directly they swim off as active *Medusæ*." Again, the tentacular muscles of the *Ctenophora* are usually smooth, only the lateral muscles of *Euplocamis*, which contract with especial vigour and rapidity, being striated. In Vertebrates, on the other hand, the bulk of the muscles is composed of cross-striated fibres, and only the sluggishly reacting muscles of the intestinal tract, urogenital apparatus, and blood-vessels, are smooth, *i.e.* exhibit no further

differentiation in their fibrils. Lastly, in the Arthropoda, which are, generally speaking, characterised by extreme rapidity of movement, all the muscles are striated, and it is just among these that we also find the most rapidly contracting fibres (thoracic fibrils of insects).

It is easy to demonstrate that the cross-striation of a muscle-cell, or fibre, depends on *the cross-striation of the single fibrils*. Each of these appears in longitudinal section as though it were regularly segmented, or, more correctly, built up of separate layers, which exhibit fundamental differences in respect of optical properties, and affinity for staining, as indeed of all chemical and physical reactions. This construction is most evident in the thick, thoracic fibrils of insects, and in the bundles of fibrils known as "muscle-columns," which, in consequence of the regular juxtaposition of the single—often excessively fine—fibrils exhibit precisely the same transverse banding as that which we ascribe in this instance to each elementary fibril. The optical appearance of the striation is in general a regular succession of light and dark bands, which lie one above the other like coins in a rouleau. Such a series of striæ may be very complicated in detail, since a whole system of light and dark parts can be grouped together, as it were, in a higher unit; the regular, periodical alternation of the individual segments is, however, a persistent characteristic. The separate bands—as will be shown below—present quite a different appearance in the resting and in the contracted condition. The arrangement in *the resting state* will be first considered.

Both in Vertebrates and Invertebrates, the relaxed, striated muscle-fibre, or bundle of fibrils, exhibits broad, dark, transverse bands under an appropriate power of the microscope, separated again by smaller, clear bands; these last, in suitable preparations, can at once be recognised as the expression of the regularly juxtaposed, homogeneous segments of the fibrils, of which the muscle-fibres, or muscle-columns, consist between every two transverse planes of the fibre. In the simplest cases, each dark band appears to be divided in the middle by a faint, clear line, each light band by a dark line (Fig. 27, *I*, *h* and *Z*). In many cases, however, *e.g.* in the Arthropod muscles, the segmentation is much more complex (Fig. 27, *II* and *III*). It is convenient, with Rollett, to indicate the individual segments of the fibrils, or the

transverse bands or stripes to which these give rise in the entire fibre, by a system of letters. The large sections (*Q*), which appear dark on lowering the objective, are divided by the band (*h*), which is *light* with the same focus, of varying breadth, and not usually well defined, into three parts—the two “dark bands” (*Querschichten*), and the less strongly refractive Hensen’s stripe (“*Hensenche*” *Mittelscheibe*, *h*), which is not always visible. Schiefferdecker gives the name of “middle band” (*M.* “*Mittelschicht*”) to a very fine dark line, first accurately described by Hensen, which sometimes appears in the “middle stripe” (*h*), but is not always visible. The segments (*Q*) are generally longer

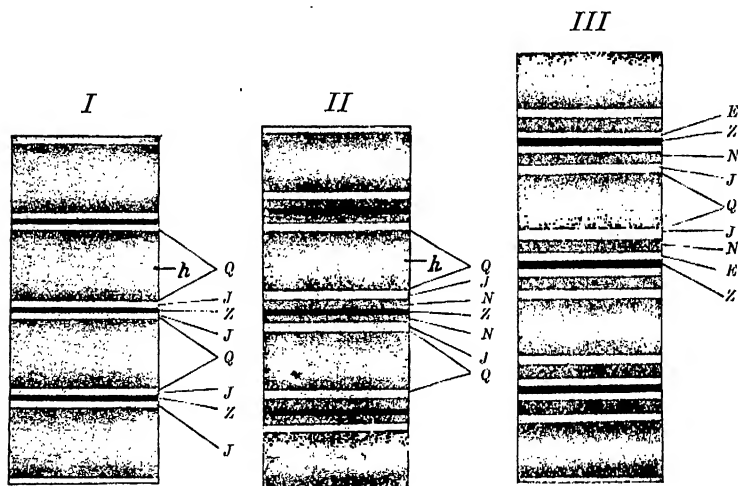


FIG. 27.—Schema of the transverse striation of Beetle-muscle. (Rollelt.)

in Arthropod muscles than in Vertebrates, so that, with the coincident longitudinal striation, the muscle-fibres look as if they were composed of long, dark rows of granules (Fig. 31). The dark band which bisects the clear segment with a low objective (as described by Amici) is known as Dobie's line (*Z. Zwischenschicht*, Engelmann's "*Zwischenscheibe*"). Krause described this band as the "transverse line" and "basal membrane" of his "muscle-cases" (*infra*). Between (*Z*) and the two *clear* segments (*J*), which in the simplest case (Fig. 27, *I*) are only separated by it, two dark bands are occasionally visible; they are very inconstant in their appearance, and are denoted by Rollett

as (*N*), corresponding with Engelmann's accessory discs ("Nebenschreiben") (Schema *II*, Fig. 27).

Finally (Schema *III*), the dark band (*N*) may appear in the middle of the clear segment (*J*), so that Dobie's line (*Z*) is bordered directly on either side by a clear line (*E*), followed by (*N*), and then by another clear line (*J*), so that the entire system of bands in a fibre-segment enclosed between two Dobie's lines (*Z*) is as follows:—(*Z E N J Q J N E Z*); the next simplest case is (*Z N J Q J N Z*); the simplest of all (*Z J Q J Z*). It is important to remember that none of these several systems of striæ can be regarded as characteristic of *all* muscle-fibres in any particular species of animal. On the contrary, the three conditions of striation indicated in the figures may occur in *one and the same* fibre, and merge into one another, as shown by Engelmann in the muscles of insects in particular. This effect is due in the first place to different conditions of contraction in the fibres; the most complicated kind of cross-striation always corresponding with the greatest relaxation of fibre. This by no means excludes the possibility of specific varieties of striation; all the observations tend to show that if it were possible to investigate the muscle-fibres of different animals, or the different muscle-fibres of the same animal, when perfectly relaxed, or at the same degree of extension, they would present very different appearances.

The reaction of striated muscle-fibres, or individual layers of fibrils, and of the sarcoplasm, to different reagents, is extremely interesting both morphologically and physiologically,—the differences exhibited being no less striking than in regard to optical properties. This is plainly expressed by the different colorability of the individual segments. If the transverse section, or the entire muscle-fibre, is appropriately treated with hæmatoxylin, we find that only the contractile, fibrillated substance of the muscle-columns stains in the first case, and not the interstitial sarcoplasm. On comparing good hæmatoxylin preparations of muscle-fibres in longitudinal section, it is evident that only the segments (*Q*), (*N*), and (*Z*) are stained, while the intermediate spaces between them (*i.e.* the sarcoplasm) and the striæ (*h*), (*J*), and (*E*) are almost or wholly unstained.

It has been shown that the gold chloride method under certain conditions gives an opposite reaction; the sarcoplasm only stains, while the contractile fibrils embedded in it remain uncoloured.

Hence in cross-section (Biedermann, Thin, Gerlach, Retzius, and others), Cohnheim's areæ stand out colourless from the very distinct red plexus of the sarcoplasm. The longitudinal section of fibres treated with gold is no less divergent. Gerlach, who investigated vertebrate muscle only, characterises it as "speckled"; each fibre appears interspersed throughout its thickness with a crowd of dark, red or black, dots and streaks, which, as Gerlach correctly observed, give an impression of continuous and often varicose fibres in places, and are only too easily mistaken for fine nerve-fibrils (Fig. 28). The gold chloride figures of Arthropod muscles are generally much more regular, and accordingly present less ambiguous conclusions.

Before discussing these facts, it is advisable to consider briefly the simple action of acids, since this is always combined with the gold method. The first effect of treatment with very weak acids (acetic, formic, haloid, etc.) is best exhibited in muscle-fibres which have lain in strong alcohol (93 %) for twenty-four hours. The earliest and most striking changes occur within the system of striae (*Q h Q*), which swell up, and seem to bulge out from the wall of the fibre (or muscle-column). This process may go so far, on applying a somewhat stronger solution, as to effect radical alteration in the striae (*N Z*), which lie, as it were, crushed in between the much-broadened and now homogeneous (*Q*) bands (Fig. 29).

On the other hand, the rapid swelling of the segments (*Q h Q*) at a still more advanced stage of the acid reaction may produce an explosive disintegration of the muscle-fibres into discs, by a process of continuous splitting up within (*Q*), by which the segments (*JNE, Z, ENJ*) are finally driven apart, and isolated as discs. It would follow that the changes which the longitudinal section of the muscle-fibre undergoes during the action of strong acids are to be referred partly to changes of form in the muscle-columns (or fibrils), due to differences of turgescence in the indi-



FIG. 28.—Surface of muscle-fibre (Frog) treated with gold chloride to show Gerlach's "speckles." (Biedermann.)

vidual segments of the fibril, accompanied by changes of refractibility; partly, however, to the sarcoplasm, which also undergoes changes both in respect of local distribution and of refractibility.

Since the individual segments of the fibrils, or muscle-columns, swell in different degrees, so that each element appears alternately thickened and constricted (a form frequently observed by Rollett in fresh, spontaneously contracting muscle-fibres), it is evident that the sarcoplasm which separates the muscle-columns

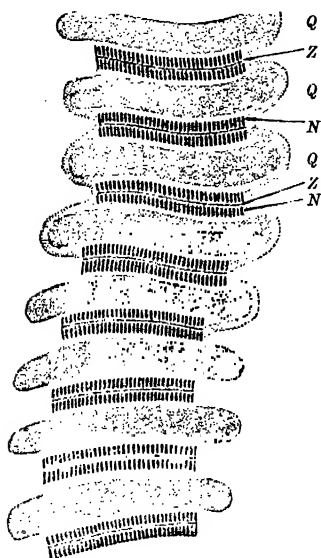


FIG. 29.—Muscle-fibre of *Aphodius rufipes* (alcohol) splitting into discs after treatment with weak acid; swelling of Q layers. (Rollett.)

must be partially driven out of the interstitial spaces of the swollen sections, while it accumulates in the interstices of the narrowed sections. Remembering further that the substance of the fibrils (muscle-columns) is clear in acid, swollen muscle, while the sarcoplasm is dark (as in the normal fibre with a high adjustment), the explanation of the acid reaction is very simple.

The acid figures described correspond (as Rollett shows) in all essential points with the gold chloride figures, except that in the latter the darker knots of sarcoplasm, as well as the connecting lines, which result from the impregnation of the metal, are more or less intensely coloured, while the fibrillated substance is unstained, so that the

longitudinal section of the fibre gains considerably in clearness and precision.

Another kind of discoid disintegration (differing essentially from the above) was first described by Bowman, and has recently been reinvestigated by Rollett, in the muscles of insects. This is a peculiar action of strong alcohol (93 %), in which the muscles have been steeped for some time (twenty-four hours to fourteen days). The figures obtained under these conditions are very characteristic (Fig. 30).

In fibres where the cross-striation corresponds with the simplest schema ($ZJQhQJZ$), the segments (QhQ) are found as trans-

verse discs, which are either completely isolated, or still lie within the sarcoplasm; this last is more or less swollen, and divided by delicate partition walls, corresponding with the segment (*Z*), into solitary cases or compartments arranged in longitudinal series, each case containing a transverse disc, corresponding elsewhere with the system of striæ (*N J Q h Q J N*). It is to be noted that the segments (*Q h Q*) do not swell out as in the acid reaction, but are only separated by alterations within the segment (*Z*). The sarcoplasm appears to be constricted at the junction of the partition walls, while the cases between bulge outwards.

Bowman explains this bulging, which is visible before the final breakdown into discs, by the withdrawal of the sarcolemma from the surface of the discs, to which it adheres firmly.

Rollett, on the contrary, observes with justice that it is not merely the sarcolemma that shrinks, but also a portion of the sarcoplasm, which covers the inner side of the sarcolemma in a sheet of varying thickness, so that we are dealing with a local vacuolation of the muscle substance.

Our own experiments lead us to accept Rollett's explanation of the alcohol disintegration into discs as entirely satisfactory. He assumes that the endosmotic pressure of the fluid in the circular canals originally present in the muscle increases considerably, but that the segment (*Z*) possesses a certain firmness and resistance, while the impinging layer (*E*) or (*J*) is very yielding, and therefore liable to maceration from the fluid. This results in the freeing of the intermediate layers as a disc within a compartment, the walls of which are formed above and below by a segment (*Z*), at the sides by the bulging of the primitive canal. The peculiar resistance of the segment (*Z*) had already been discovered by Engelmann.

The figures which arise from this discoid disintegration of the muscle-fibres might, of course, be interpreted on the theory

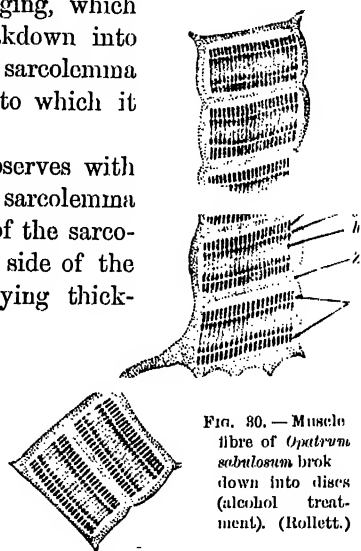


FIG. 30. — Muscle fibre of *Opatrium sabulosum* broken down into discs (alcohol treatment). (Rollett.)

of W. Krause, that every muscle-column is composed of strata of "muscle-cases," which in juxtaposition form the "muscle-compartments" of the entire fibre; each muscle-case, bounded beneath by (*Z*) the "basal membrane," contains, as well as fluid corresponding with (*J*), a "muscle-prism," represented like the Bowman "discs" by the (*Q h Q*) system of striæ. Krause only takes account of the fibrillated structure of the muscle-fibres, in so far as he assumes the muscle-prism to consist of *muscle-rods* (Bowman's "sarcous elements"), which, according to the description given above, correspond with the segments of fibrils (*Q h Q*) only. The untenability of this theory, according to which not fibrils, but muscle-cases, are the elementary constituents of the muscle-fibre, is obvious from the facts we have stated; the breakdown into discs within the segment (*Q*) in the acid reaction is very convincing evidence against it. Nor is there any better justification for the muscle-elements of Merkel, which are each bounded by two (*Z*), in this case necessarily assumed to be divisible. This is not the place to enter into the many other systems (including Bütschli's "cell theory") that have been elaborated from time to time, in regard to the much disputed finer, and finest, structures of striated muscles.

We have already had frequent occasion to refer to the *optical properties* of muscle-fibrils, especially in striated muscle. Even when examined in ordinary light the different segments of the striated fibrils exhibit a very different refractibility; it may indeed be said, with reference to Rollett's system of indicating the individual segments, that all the bands denoted by consonants are more highly refracting, and also doubly refracting (*anisotropic*) although in very different proportions.

As was said above, the bands (*Z*) and (*N*) appear much darker than (*Q*) with a certain (low) power of the microscope, and it is owing to the strong refractibility of (*Z*) in particular that it is easily recognised even in imperfect preparations. The striæ denoted by the vowels (*J*) and (*E*), as well as (*h*), are, on the other hand, less refractile and singly-refracting (*isotropic*); these, under conditions which make the bands denoted by consonants appear dim, will be clear and inverted. The doubly-refracting property of striated muscle-fibres was discovered by Beck in 1839, but Brücke in 1857 was the first to examine it minutely.

Under a polarising microscope, with crossed Nicol prisms, the anisotropic bands (*ZN*) and (*Q*), which look dark in ordinary light, with a low objective, appear clear and shining, standing out sharply in a dark field, while the isotropic bands (*JE*) and (*h*) remain dark under the same conditions. Very beautiful figures are exhibited by muscle-fibres in polarised light when the field of vision is coloured by a mica or gypsum plate of corresponding diameter. The anisotropic layers stand out vividly in the complementary colours, according to the direction of the fibres. Light falling parallel with the long axis of the fibrils is singly refracted. With crossed prisms a transverse section, if sufficiently vertical to the fibre axis, remains dark in all its parts and at all azimuths, and does not change colour anywhere with a gypsum background.

The anisotropic portions are also uniaxial. Brücke ascertained that they were positive by means of a movable quartz wedge; each muscle-fibre acts like the thick end of a quartz wedge when lying parallel to its axis, and is therefore positive like quartz.

Rollett has recently applied the spectrum analysis of polarised light to this investigation, and has confirmed, with the "spectro-polarisator," the earlier observations of Engelmann, viz. that (*Z*) and (*N*) are less positively doubly-refracting than the less refractile segment (*Q*). At the same time the remarkably clear and sharp figures obtained with this method leave no doubt that the accessory discs (*N*) are just as much due to doubly refracting segments of the fibrils as (*Q*) or (*Z*). All the intercommunications of sarcoplasm, on the other hand, look quite dark polarised light, so that the doubly-refracting segments of the muscle-columns in the longitudinal section of the fibre "lie completely isolated on a dark field in regular series close to one another."

Engelmann (2) has remarked that double refractibility is a widely distributed property of contractile protoplasm, appearing even among protozoans. The stalk muscle of *Vorticella*, *e.g.*, exhibits strong double refraction, and the fibrils behave exactly like the fibrils of striated muscle, *i.e.* are uniaxial, with the axis parallel to the longitudinal direction of the fibres. In *Stentor*, the cortical layer of plasma is usually doubly-refracting throughout its diameter, as well as the muscle-fibrils; double refractibility is also very conspicuous in the rays of *Actinospherium*,

where each plasma ray acts like a doubly-refracting fibre with one optical axis, which is parallel to the longitudinal direction of the fibre, and therefore, generally speaking, with the direction of contraction in the plasma. The same properties also characterise the fibrils of the epithelial muscles of Hydra. The behaviour of the bi-obliquely striated muscle-cells of many vertebrates in polarised light is also remarkable. According to Engelmann, *e.g.*, "the optical axis of the fibrils does not coincide, as might be expected from analogy, with their longitudinal direction, but invariably with the long axis of the muscle-fibres": the latter, no matter what angle the fibrils form with the fibre-axis, are always at maximum clearness, provided the axis lies at an angle of 45° to the plane of polarisation between the crossed Nicol prisms.

Double refractibility therefore appears as a characteristic property wherever the contractile particles of plasma lie permanently *in a definite direction*, and moreover seems invariably to denote uniaxial particles, whose optic axis coincides with the direction of contraction. The striated fibrils must, with Engelmann, be regarded as consisting mainly of an isotropous basal substance, running longitudinally, in which the doubly-refracting particles (which must be regarded as the seat of the contracting forces) are arranged in regular striæ, corresponding with the metabolous segments.

It remains to give a brief account of the changes in cross-striation which take place during the contraction of the muscle-fibre, since they are of almost equal morphological and physiological interest. As we learn by observation, the changes of form in fibre, or fibril, of the muscle are a shortening and a thickening; and this of course not merely in the entire fibril, but in each individual tract of the same, and each individual segment.

If the attention is fixed on a contracted spot in a living fibre, *e.g.* in insect muscle, which frequently exhibits short waves of contraction, with relatively low velocity, long after preparation, it is easy to distinguish two kinds of transverse bands within the wave; one small and invariably dark, the other clear and somewhat broader. The contracted fibres therefore present on the whole an aspect similar to the resting fibres, *i.e.* a regular alternation of dark and light cross-bands, only the single striæ are much closer together, the dark bands much smaller than in the relaxed fibre.

It is also easy to see that the dark, sharply defined bands appear where the relaxed muscle presents the segments, (JZJ), or (JNE, Z, ENJ), and that the light bands correspond essentially with the contracted striæ (QhQ).

The muscle-fibres of insects, killed by strong alcohol, often exhibit local contractions ("fixed waves of contraction") in which the histological changes produced in the striated fibrils during the transition from rest to contraction can be ascertained exactly by means of staining methods and reagents. These very subtle manifestations are of the greatest theoretical interest, and must be discussed a little more fully.

As before, we may accept the penetrating conclusions of Rollett (22). On examining a well-fixed wave of contraction, from a fibre of *Otiorhynchus mastix* stained with hæmatoxylin (Fig. 31), it is in the first place evident that the dark-blue band (C) of the contracted portion of the fibre, Nasse's "contraction-disc," is derived from the transformation of the system (JNE, Z, ENJ), and is therefore the same section which Engelmann denotes as *isotropous*, and Rollett as the *arimetabolous* layer (a).

In the relaxed arimetabolous layers the bands (Z) and (N) are deeply stained, the bands (E) and (J) not at all, or very slightly; in the relaxed "metabolous" sections (QhQ) (Engelmann's "anisotropous" layer), which Rollett denotes by μ , the ends of Q are more deeply stained than the centre h (Hensen's stripe). With increasing contraction of the section (a), the diminishing bands (N) draw nearer and nearer to (Z), until at last the two

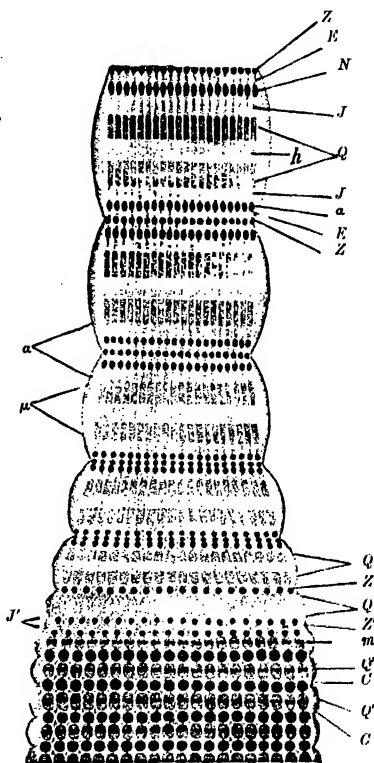


FIG. 31.—Muscle-fibre of *Otiorhynchus mastix*, showing wave of contraction. (Rollett.)

(*E*) lines between (*N*) and (*Z*) can no longer be distinguished, as is the case at the outset in the less richly striated fibres. A striking change occurs in the next stage within the (*a*) system. Instead of the colourless segment (*J*) two strongly-coloured bands appear, while a clear stripe takes the place of (*Z*) between them. Rollett denotes the former by (*J'*), and the latter by (*Z'*), since they are undoubtedly derived from (*J*) and (*Z*), as appears particularly from their behaviour in polarised light—the dark (*J'*) like the light (*J*) is singly refracting, while the clear (*Z'*) like (*Z*) is doubly refractile. When, as sometimes happens before the last stage is completed, the segments (*J'*) are not yet quite dark, the segments (*Z'*) on the other hand not quite light, so that they resemble each other, the muscle-fibres meeting at the points of the contraction wave exhibit most indistinct cross-striation; this is the so-called *homogeneous* stage of earlier authors, forming the transition to the system (*J'*) and (*Z' + J'*), which again represents the commonest transition to the series of bands in the completely contracted muscle. While the clear (*Z'*) is disappearing between the dark (*J'*), these in their turn melt into the “contraction-band” (*C*), as described by Nasse, which is highly refracting, very dark, and intensely blue, in the hæmatoxylin reaction. It obviously corresponds with the system (*J + Z + J*) or (*J + N + E + Z + E + N + J*) of the relaxed and resting fibres, from the transformation of which it has arisen.

The changes within the (metabolous) segments (*Q h Q*) are at first less striking, and the contraction is also smaller. Later on the band clears up, the difference between the darker (*Q*) and (*h*) grows less and less, and finally a dark, ill-defined band (*m*, Rollett) appears in place of the latter. Rollett denotes the entire series of altered segments (*Q h Q*) in the contracted fibre by (*Q'*). The transition from relaxation to contraction in a fibre often proceeds much more slowly than in the example described above; the single stages may extend over several segments of the fibres, an effect which only enhances the clearness of these figures.

Polarisation phenomena during contraction are not easy to follow on fresh muscle-fibre, but Rollett (22) was able to assure himself of a diminution of the double refractibility, a fact that can also be ascertained from fixed waves of contraction, and had been previously conjectured by Engelmann (23) (cf. Ebner, 24, p. 233). It is directly apparent from the fact

that muscle-fibres exhibiting such fixed waves of contraction, when considered on a gypsum ground in the plus and minus condition, exhibit no particular alteration of colour in the contracted as compared with the relaxed parts, although normally increase of bulk in a muscle-layer does perceptibly deepen the colour, *e.g.* when two relaxed fibres partially cover each other. Even high waves of contraction exhibit, in comparison with the relaxed portions of the fibre, little or no alteration *qua* increase or decrease of colour, in the ascending or descending stages.

This leads us to infer that in contracted muscle-fibres the increase of colour which should go along with the thickening of the fibre is compensated, or over-compensated, by a diminution of the double refraction coincident with the contraction.

The method of polarised light enables us further to form a conclusion with regard to another important point in the behaviour of striated muscle-fibres during contraction. If the height of the metabolous and arimetabolous segments is compared in an appropriate preparation (Fig. 32) with crossed prisms, during the transition from the relaxed to the contracted portions of the fibre, it may be seen that with increasing contraction the height of the isotropous (arimetabolous) segments diminishes more than that of the anisotropous (metabolous), so that the volume of the latter increases at the expense of the former, the total volume of the section in question, like that of the entire fibre, remaining constant. Engelmann has established these facts in appropriate objects by micrometric measurements. In order to explain the effect he assumes that fluid passes from the isotropous to the anisotropous substance in contraction; the anisotropous substance swells, the isotropous shrinks. This water-exchange between the metabolous and arimetabolous segments must naturally be imagined as between the elements of the muscle-column, or single fibril, corresponding with these segments. An inverse change in volume occurs upon relaxation, and the surplus of fluid returns to the isotropous (arimetabolous) system. This theory is

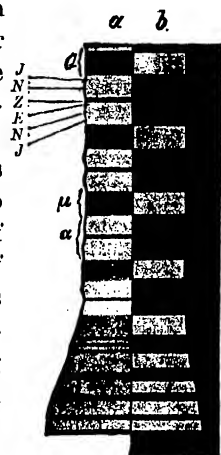


FIG. 32.—Muscle-fibres of *Telephorus luridus* in traction. *a*, in ary; *b*, in pol light. (Engelmann From Foote's *Text-Book of Physiology*.)

not only supported by the changes in volume (*supra*) of the two chief systems of segments in each fibril, but is also confirmed by the diminution of double refractibility already mentioned in contraction, as well as by the fact that under these conditions the isotropous (arimetabolous) bands appear darker and less transparent. The anisotropous, on the contrary (with the exception of the middle disc), is clearer and more transparent in ordinary light. In proportion as the segments (*Q*) (dark bands) imbibe water from the isotropous system, they must become not only more voluminous, but also less refractile, and clearer, as well as less doubly-refracting. The isotropous bands, on the other hand, would become smaller and more refractile, and darker in appearance, as is actually the case. Finally, the alterations in colour of the contracted section of the fibre agree well with the theory that the anisotropous segments swell at the expense of the isotropous. The colourability of turgescient bodies, as well as their chemical constitution, is known to depend in great measure upon the degree of turgor at the moment. The rule for each single, turgescient, colourable mass is that it stains the more intensely in proportion as it contains less water of imbibition. As a matter of fact, increased colourability of the arimetabolous (isotropous) bands can be observed during contraction, while the metabolous (anisotropous) segments stain much less deeply with hæmatoxylin than during the resting state.

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CHAPTER II

CHANGE OF FORM IN MUSCLE DURING ACTIVITY

SOME of the manifestations concomitant with activity in the muscle, *e.g.* the resulting changes in optical properties, have been described in the previous section. The chemical constitution of muscle-substance, and its alterations in activity, can best be studied in recent text-books of Physiological Chemistry. There remains for consideration the most striking manifestation of muscular activity, *i.e.* *change of form (contraction)*. The most essential feature—*contraction in a longitudinal direction with simultaneous expansion* (increase of cross-section)—appears, as a matter of course, in all cases where the contractile particles of protoplasm lie permanently or temporarily in a definite direction. This has already been pointed out *re* the more or less rapid, sometimes instantaneous, shortening and thickening of certain forms of pseudopodia (*Myopodien*, *Myophrysken*), as well as in the myoid layer, or myonema, of certain infusoria, which must be regarded as true muscle. Indeed, the same changes of form may be observed, as it were, in an elementary stage in single fibrils, or bundles of fibrils, that reappear in the highly-complex, multicellular organs which it is usual to designate as muscles in more highly-organised animals. In every case the mechanical effect of change of form in a muscle depends upon its *shortening* in a longitudinal direction—never upon its *thickening*. Hence it is customary only to speak of shortening, or contraction, with reference to muscle-activity.

We have already stated in discussing the manifestations of activity in the myoideum that a single stimulus of very short duration, *e.g.* a single, quick alteration of density in an electrical current, or the shortest possible mechanical impact, produces an

equally rapid contraction, with much slower subsequent elongation. A rapid contraction of this kind, which is especially characteristic of striated muscle, is termed a "*twitch*." This elementary form of activity is, however, by no means peculiar to muscle, since, on the one hand, the rhythmical, or even non-rhythmical, movements of a ciliated element may be regarded as consisting of single, consecutive twitches, many flagella also "twitching" in contraction; and, on the other, many muscles—the uninuclear, smooth muscle-cells in particular—contract so slowly that it is as impossible to speak of "twitch" in these as in the far more sluggish contraction of the pseudopods in most Rhizopoda.

A "twitching" contraction seems invariably to denote the presence of fibrillated structure (more especially with cross-striation), although, as we see in smooth muscle-cells, the differentiation of fibrils does not on the other hand invariably produce a very rapid contraction.

In the most characteristic case of the "twitch," contraction, as far as can be seen, begins simultaneously with the cause of excitation, reaches its maximum as quickly as possible, and then dies out again in *slow* relaxation. The very marked difference which appears between the duration of contraction on the one hand, and elongation on the other, in the contractile, twitching parts of the lowest animal-forms (stem of vorticella, spirostomum, myopodia, etc.), is due in great part to the peculiar mechanical relations which here govern contraction and relaxation. The twitching fibrils behave more or less like an unloaded muscle, swimming in mercury, which only recovers its normal length when an extending force is acting upon it. The course of a single twitch is usually so rapid that it is impossible, from direct observation, to detect any minutiae in regard to the time-relations of the contraction, and behaviour of the contractile fibres, in the individual stages of shortening. Finer artificial means of measuring time are necessary in order to ascertain the relations of the different phases within the brief act of a single contraction.¹

As a means of measuring such minute intervals as are here under consideration, preference must undoubtedly be given to the

¹ Cf. v. Bezold, *Untersuchungen über die elektrische Erregung der Nerven u. Muskeln*, 1861, p. 31. (Historical survey of attempts to measure the minute time-intervals occupied by nerve and muscle action.)

graphic tracing of the process to be measured, upon a rapidly-moving surface. If such a surface (of smoked glass or paper) moves with sufficient velocity past the point of a recording lever attached to, and following the contraction of, the twitching muscle to which it is attached, a curve is obtained, the abscissa of which corresponds with the time, the ordinates on the other hand with the magnitude of the contraction (expansion) of the muscle. This is the principle of the *Helmholtz Myograph*, which has been followed by a number of similar instruments, as described in every text-book.

The time value of the abscissa in every such "contraction curve" is easily determined if the speed of the travelling-surface is known, or if a tuning-fork tracing is taken simultaneously with the "myogram."

The application of the graphic method enables us at once, and simultaneously, to recognise the peculiarities characteristic of the



FIG. 33.—Curve of muscular contraction. (Helmholtz.) *a*, Moment of excitation.

process to be examined, in *magnitude*, *form*, and *duration*. If the moment of stimulation is marked upon the recording surface, the rise of the lever from the abscissa does not usually coincide with the moment of stimulation, but occurs distinctly later, *i.e.* the muscle does not begin to shorten at the moment at which the induction shock takes effect, but a given time elapses before the charges produced by excitation bring about contraction, as expressed in the movement of the lever (Fig. 33).

The length of this time, measured between *a* and the beginning of the curve along the abscissa, was estimated by Helmholtz at about 0.01 sec. for a loaded frog's muscle directly excited by an induction shock. It is known as the period of latent stimulation (latency period), because during this time no visible mechanical effect is produced by the stimulus. Contraction of the muscle begins when the discharging stimulus has ceased, and is marked by the rising of the lever to the summit of the curve. From

this point the muscle lengthens slowly until it reaches its original dimensions. The interval between the beginning of the contraction and its maximum is known as the period of rising energy, that from the maximum to complete extension of the muscle as the period of falling energy; the entire period from the beginning of the contraction to complete extension represents the duration of the contraction.

In regard to the amplitude, or height, of muscular contraction, it must be remembered that there is generally a more or less considerable enlargement in graphic records, and that the length of the recording lever must always be taken into consideration, if the real magnitude of contraction is to be determined. The two stages of rising and falling energy may easily be determined if an ordinate is drawn from the top of the curve, vertical to the abscissa. As a rule the first is distinctly shorter than the second, but the opposite may occur (e.g. on cooling). With regard to the form of the contraction curve it must be remarked that in many instances we cannot regard it as a complete expression of the process of movement, since the recording lever is frequently arranged (apart from possible spontaneous variations) so that its point describes the arc of a circle in moving. The velocity of the travelling surface has also a considerable effect upon the form of the curve—one and the same movement, recorded by the same lever, yields very different curves, according as the myograph plate travels fast or slowly.

I.—DEPENDENCE OF THE PROCESS OF CONTRACTION UPON THE NATURE OF THE MUSCLE

The marked differences which exist in regard to the rate of movement as manifested in different kinds of protoplasm, lead us *a priori* to anticipate that similar distinctions must exist in the muscles of different animals as well as in the different muscles of the same species, as might be inferred at once from their fundamental differences of structure. And indeed the merest glance shows that without considering other external influences yet to be mentioned, the form and process of contraction are essentially dependent on the nature of the muscle. Above all, we are impressed by the enormous difference exhibited between *smooth*

muscle and *striated muscle*. The contractions of smooth muscle are incomparably slower than those of striated muscle, so that we could never speak of a "twitch" when a single stimulus was acting on the elements of smooth muscle. The entire course of contraction is, so to speak, macroscopic, since the latent period, as well as all the phases of contraction and elongation, can be conveniently followed by the eye without artificial assistance.

Midway between these sluggishly contracting smooth muscles and the "twitching," striated muscles of invertebrates and vertebrates stand the uninuclear, cross-striated elements of *cardiac muscle*, where contraction is neither so sluggish as in smooth, nor so rapid as in most striated skeletal muscles. For this reason it was long a matter of dispute whether the single contraction of the heart, discharged by a momentary excitation (which in no way differs from a natural "heart-beat"), is really comparable with the elementary single twitch of a skeletal muscle. But that it is so cannot now be doubted. It is clear that its longer duration is no sort of proof that the single contraction of cardiac muscle does not correspond with a simple twitch. Even among the striated skeletal muscles of different animals, or the muscles of the same individual, considerable differences may occur, as we have seen, in regard to rapidity of contraction, and it is easy to produce these artificially to a much greater extent than is the case in normal cardiac contraction.

We shall therefore assume that *every single contraction of cardiac muscle (vertebrate or invertebrate), whether natural or produced by a brief artificial stimulus, is an elementary "twitch," although retarded and protracted in all its phases.*

If, under approximately equal conditions, the contractions in the heart and skeletal muscle of the frog, excited by a single induction shock, are recorded by the graphic method with a lightly attached lever, it will be found, as Marey pointed out (1), that the heart-curve and muscle-curve exhibit in respect of form the same characteristic peculiarities of rapid rise, and more gradual sinking.

The latent period is, however, without exception, longer in cardiac than in skeletal muscle under the same conditions, and the more conspicuously so in proportion with the difference in rapidity of contraction between the two kinds of striated muscle. As this difference is greater in poikilo-thermic vertebrates than in the

warm-blooded animals, the difference in the length of the latent period is more marked also. Thus in the frog the latent period of cardiac muscle may last 0.28 sec., while in the gastrocnemius of the same animal it is only 0.01 sec. according to Helmholtz, and still shorter (0.005 sec.) according to the latest observations. The period of rising energy is, in the frog's heart, 2-3 secs. according to Marchand (2), while the same period in skeletal muscle must be measured by fractions of a second. The striated muscles of the medusæ, which approximate to cardiac muscle in other respects also, are characterised by a similar sluggish contraction (Romanes, 3).

Similar, if less extensive, differences in the time-relations of contraction have recently been shown to exist within striated skeletal muscle itself, and that not merely in different animals, but in one and the same individual, even within one muscle. *It may be said, speaking generally, that there are, in a physiological sense, two kinds of multinuclear, cross-striated muscle-fibres, characterised respectively by rapid and by sluggish contraction ("quick" and "sluggish" muscles).* Between the two there are innumerable intermediate stages.

It is, e.g., evident that the skeletal muscles of a tortoise or chameleon, as a rule, contract much more slowly than those of the frog or a warm-blooded animal; while, on the other hand, certain muscles of insects contract more quickly than the best-adapted muscles of warm-blooded animals. This is practically obvious from the respective movements of the creatures, taking only, e.g., the slow sluggish movements of the tortoise in comparison with the marvellously rapid wing-beats of many insects, whose muscle-fibres must contract several hundred times in the second. The contraction curve of such muscles must be immeasurably shorter than that of the frog or tortoise. It is probable that, as Hermann (4, p. 38) suggested, a continuous, graduated scale might be drawn up in the animal kingdom, beginning, after Marey, at the excessively rapid contractions of the wing-muscles of insects; then would follow the striped skeletal muscles of birds, fishes, mammals, frogs, toads, and lastly of tortoises and hibernating dormice, then cardiac muscles, and finally most of the smooth muscle-cells whose contraction process, as we have said, is macroscopic. In frog muscles the single twitch lasts, at ordinary temperature, from 0.1 to 0.3 sec., in the tortoise often more than 1 sec., while in

the wing-muscles of many insects the duration of a contraction falls to $\frac{1}{300}$ sec., lasting, on the other hand, for several seconds in smooth muscle. Hand in hand with these differences in the period of contraction are other differences in the size of the mechanical latent period, which, as a rule, increases with increasing duration of contraction.

The fact that the striated muscles of the same animal may present very important functional as well as histological and chemical differences, is very interesting. Ranvier (5) was the first to observe that the contraction period differed in the pale and red muscles of the rabbit, the red being distinguished from the pale muscles by a comparatively long contraction period, and a corre-

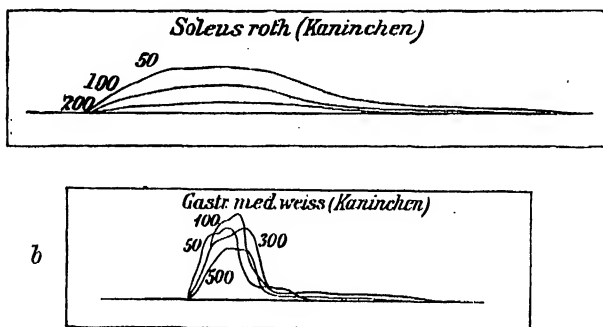


FIG. 34.—a, Three maximal contractions loaded at 50, 100, and 200 grs.; b, four maximal contractions at 50 to 500 grs. (Cash.)

spondingly longer mechanical latent period; the pale muscles contract much more quickly after a short latent period. In particular, Ranvier compared the function of the red semitendinosus muscle with that of the pale vastus internus, or adductor magnus, in rabbit, and found on stimulating with single induction shocks that it did not contract quickly like the pale muscle, but shortened gradually, the latent period being four times greater. Kronecker and Stirling (6) confirmed these facts, finding the contraction period of red muscle nearly three times as long as that of the pale, while the height of contraction of the former was quite insignificant as compared with the pale muscle (Fig. 34, a, b). Marey had made similar observations on the different muscles of the frog, finding, e.g., that *M. hyoglossus* was more sluggish than *gastrocnemius*. Cash (7) ascertained by conclusive experiments

that in both the frog and tortoise different muscles are distinguished by characteristic differences in the form and process of the curve of contraction. The average duration of contraction in different skeletal muscles of the frog is shown in the following table:—

	Sec.
1. <i>M. hyoglossus</i>	0.2–0.3
2. „ <i>rectus abdominis</i>	0.17
3. „ <i>gastrocnemius</i>	0.12
4. „ <i>semimembranosus</i>	0.108
5. „ <i>triceps</i>	0.104

Cash found the contraction period of *Testudo europæa* to be:—

	Sec.
1. <i>M. pectoralis major</i>	1.8
2. „ <i>gluteus</i>	1.6
3. „ <i>palmaris</i>	1.0
4. „ <i>gracilis</i>	1.0
5. „ <i>biceps</i>	0.9
6. „ <i>splenius capitis</i>	0.9
7. „ <i>triceps brachii</i>	0.8
8. „ <i>retrahens colli</i>	0.75
9. „ <i>semimembranosus</i>	0.6
10. „ <i>omohyoideus</i>	0.55

Yet more characteristic than the duration is the nature of the process (*form*), as expressed in the myograms. Many of these have such significant forms that they ought in a measure to indicate the species of muscle. The accompanying figure (Fig. 35A) shows how differently *gastrocnemius* behaves from the *triceps* and *semimembranosus-gracilis* group. These last muscles reach the maximum of contraction soon after the half of their entire contraction period, while *gastrocnemius* takes two-thirds of its period for contraction, and only one-third for extension. If the following group of the most sluggish frog muscles (Fig. 35B) is compared with these curves, the difference is very striking.

Fig. 35C of tortoise is even better qualified to show how the contraction curves of different striated muscles may vary in form in the same animal. *M. omohyoideus* contracts most rapidly in correspondence with its function of withdrawing the head of the animal quickly under the protecting carapace when in danger, while the powerful *pectoralis major*, which serves the movements of the heavy animal, “begins with an energetic lift, and delays some time at the apex of contraction.” Similar differences should

exist between the rapidly moving eye- and tongue-muscles and the sluggish skeletal muscles of the chameleon.

It must further be remarked that both the relative and absolute height of twitch is much greater in the quick muscles in the frog than in the sluggish muscles. A rectus abdominis

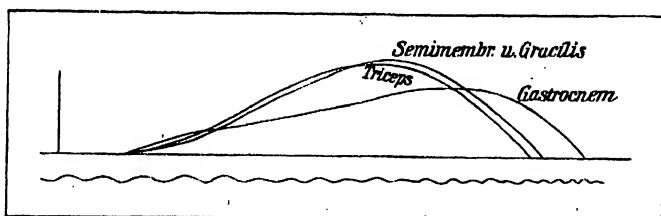


FIG. 35A.—Contraction curve of three different muscles of Frog under uniform conditions. (Cash.)

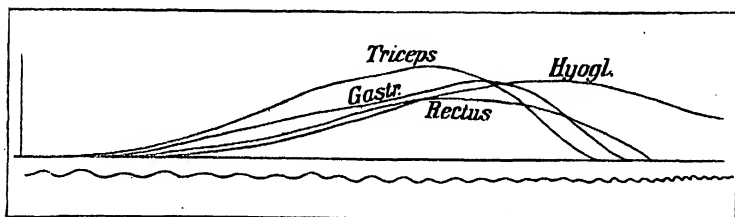


FIG. 35B.—Four contraction curves of different muscles of Frog. (Cash.)

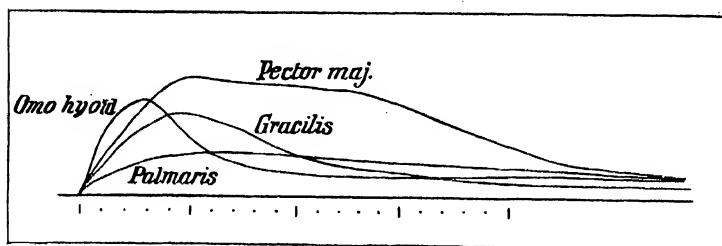


FIG. 35C.—Four contraction curves of different muscles of Tortoise under uniform conditions. The time-tracing is in seconds.

muscle of *R. esculenta*, 32 mm. long, contracted about 2.6 times less frequently at medium tension than the gastrocnemius, which was only 28 mm. long. The height of lift recorded (enlarged) amounted to 6 and 15 mm. The sluggish hyoglossus, 26 mm., has, at approximately proportional tension, a height of twitch of 1.5 mm. only (Grützner).

Rollett (8) has recently pointed out a remarkable instance of

sluggish contraction in warm-blooded muscles. We have already alluded to the peculiarities, especially the abundance of sarcoplasm, by which the striated muscles of the bat are distinguished. Experimental excitation, with single induction shocks, shows that the process of contraction in these conspicuously "dark" muscles (pectoralis major, biceps, and triceps) is remarkably sluggish. Rollett reckons an average of 0.025 sec. for the latent period, 0.146 sec. for the ascending period of the curve, 0.350 sec. for the descending period, *i.e.* 0.496 sec. for the total contraction. Hence these muscles appear more sluggish than any in the frog, but quicker than those of the tortoise, quicker than the red muscles of rabbit, but much slower than pale muscle in the same animal. The differences in the contraction process of anatomically separate muscles in the same animal are very striking also in many invertebrates. Ch. Richet (9) found very different curves of contraction in the tail and claw muscles of the crayfish, whether the contraction was discharged centrally or by artificial excitation. The curve of the tail-muscles is short, and similar to the gastrocnemius contraction of the frog. The adductor of the claw, on the other hand, described an extended curve, which differs essentially from that of the tail-muscles. This statement once more tallies with the normal movements of the parts in question (rapid flapping of the tail, sluggish but protracted closing of the claws). The greatest disparity in this direction might be expected between the wing and other body-muscles of insects, for the wide histological differences between them are an *a priori* indication of corresponding functional modifications. Unfortunately there are no adequate observations as to the contraction process in the former; it is only known that they do contract with extraordinary rapidity. Rollett has recently communicated some interesting experiments on the physiological divergences in muscles bearing the same name, but histologically different, in insects (beetles) which are otherwise very similar (10). The skeletal muscle-fibres, collectively, of *Dytiscus* differ fundamentally in structure from those of *Hydrophilus*, while each beetle possesses a perfectly uniform structure of its own muscle-fibres. *Dytiscus* exhibits in a cross-section the *flat* muscle-columns, and corresponding radial arrangement, of Cohnheim's *Areae*, from which the rays of sarcoplasm stream out featherwise from the large accumulation round the nuclei (Fig. 25). *Hydrophilus*, on the contrary,

exhibits *polygonal* Cohnheim's Areae, with a central cavity filled with sarcoplasm; each muscle-column is penetrated by a central canal, and uniformly bordered by sarcoplasm. Rollett employed preparations of these beetles, in which the muscles that work the thigh of the hind pair of legs were directly excited by induction shocks. These experiments exhibited a fundamental difference in form and duration of the single contraction in the two species. The curve of *Dytiscus* rises abruptly to the maximum of contraction, and then sinks quickly back to the abscissa. The curve of *Hydrophilus* reaches its maximum much later, maintains it for a longer time, and then sinks gradually (the myogram of cockchafer muscle is even more extended) (Fig. 36). The course of contrac-



FIG. 36.—A, Contraction curve of leg-muscle of *Dytiscus*; B, of *Hydrophilus*; C, of *Melolontha*; traced at uniform rate of the recording surface. (Rollett.)

tion in *Dytiscus* is therefore comparable with that of the pale muscle, of *Hydrophilus* and *Melolontha* with that of the red muscle, in rabbit. For the rest, the absolute duration of a twitch and its component periods varies in every case within tolerably wide limits. The following table from Rollett gives the averages of a great number of single experiments:—

Beetle.	Latent Period.	Duration of Contraction.	Ascending Portion of Curve.	Descending Portion of Curve.
	Sec.	Sec.	Sec.	Sec.
<i>Dytiscus</i> . .	0·017	0·112	0·055	0·057
<i>Hydrophilus</i> .	0·047	0·350	0·108	0·242
<i>Melolontha</i> .	0·075	0·527	0·110	0·411

If this is compared with the numbers given by Marey (11) as the possible rate of contraction per second in the wing-muscles of different insects, the extraordinary disparity of the two kinds of muscle is most clearly established:—

House-fly	330
Humble-bee	240
Bee	190
Wasp	110
Dragon-fly	28
Cabbage Butterfly	9

Again we see that the respective properties of the muscles are more or less clearly expressed in the movements of the uninjured animal.

Thus it is proved that not only the striated muscles of different animals, but those of the same species also, exhibit fundamental differences in regard to the time-relations of the process of contraction. Grützner's investigations show that the same holds good for the fibres of the single muscle also. Just as there are quick muscles and sluggish muscles, so in many, and perhaps most, cases there are quick and sluggish muscle-fibres in one anatomical muscle. As early as 1805, Ritter pointed out a physiological difference in different groups of muscles, crediting the *flexors* of the frog with a lower, "conditioned, and finite," the *extensors* with a more considerable, "unconditioned, infinite" excitability. We shall have to consider these facts elsewhere in detail; here it is enough to say that later experiments (particularly of Rollett) show that in electrical excitation of the sciatic nerve the flexors are mainly excited by weak, the extensors by stronger, currents. Grützner (12) subsequently ascertained that the flexor muscles of the frog, with direct excitation, as well as indirectly from the nerve, contract much earlier, and much more rapidly, than the extensors, as is most obvious with normal circulation and non-fatigue of both kinds of muscle.

In the first instance, this is only a further illustration of the same proposition—that different muscles of the same animal may, under certain conditions, exhibit a different contraction period, and, it may be added, different excitability. We shall have occasion to refer to yet another observation of Ranvier, according to which the triceps humeri of rabbit—consisting both of red (sluggish) and pale (quick) fibres—contracts quickly at the beginning of a long excitation series like an unmixed, "pale" muscle, owing to the greater excitability of the pale fibres, but later on, when fatigued, sluggishly, like red muscle, because the more excitable

quick fibres are more easily exhausted than the sluggish, but enduring, red fibres.

Grützner finds the same reaction in the flexors and extensors of the frog's foot. If in bloodless legs, the sluggish extensors and quick, excitable flexors are made to serve up frequent contractions, the initial difference in contraction process will completely disappear, or even reverse itself. That is to say, the flexors—composed mainly of easily excitable, quick fibres—are more easily fatigued than the characteristically sluggish, resistant extensors. This is demonstrated by the following experiment (Grützner, *l.c.*) If the iliac artery of the frog is tied on one side, the animal at first springs as if normal in the direction of its long axis, since the extensors (gastrocnemius) of both sides are able to function equally; soon, however, the animal leaves the leg of the tied side extended, and only draws it up later—after its spring—to the body: the excitability of the flexors has already been diminished by the short anæmia.

Where a single muscle is composed of two groups of fibres, differing physiologically as above, and provided the one group does not preponderate too much over the other, the contraction curve (with sufficiently strong excitation) must obviously be regarded as a combination of two curves, differing in form and time-relations, as can even occasionally be detected in the myogram. We have actually been familiar for a long time with certain peculiar double-topped curves of contraction, and their origin now becomes intelligible (13). In many cases, provided the "sluggish" fibres do not lag too far behind the "quick" fibres, they also come into play at the first excitation; the curve is double-topped from the beginning, as, *e.g.*, in the gastrocnemius group of the rat (14), and usually the frog's sartorius. In other, and indeed most, cases, where the quick fibres are in the ascendant, the mixed *fresh* muscle commonly contracts at the first effort of artificial excitation as if composed of quick fibres only—the simultaneously excited, but slower, and more sluggish portion being merely drawn along with the other. But if the quick part be more and more fatigued, the sluggish fibres come into action, and the curve becomes double-topped (15).

The difference in excitability and contraction between the quick and sluggish fibres is well exhibited in chemical excitation of the sartorius (Grützner, 16). If the upper surface

of this muscle—just beneath the skin—is moistened with a 1–2 % solution of potassium nitrate, the muscle shrinks *slowly* together; if the under surface is stimulated in the same manner there is little or no result. The whole muscle, however, contracts *instantaneously* if electrically excited by an induction shock. The cause of this striking reaction is, according to Grützner, that the sartorius of the frog consists of two layers of different muscle-fibres, of *which the upper (sluggish) layer contracts more slowly than the under (quick) layer, and while only the first is excited by the potassium salt, both, but especially the quick, react to the electrical stimulus.* So, too, many warm-blooded muscles (particularly if thin, *e.g.* muscles of belly, diaphragm), when curarised. If dabbed with salt solution they draw slowly together (peristaltic action); but if the same place is electrically excited before, or after, with an induction shock, contraction is convulsive and instantaneous. All this evidence goes to show that *a muscle, in many cases, has no physiological unity, but is a mixture of at least two functionally different elements, which, in the normal movements of the animal, serve for distinct purposes, as appears from the correspondence of the mode of movement of an organ, or single muscle, with the number of quick or sluggish fibres which characterise its movement.* It is also instructive that (as Rollett pointed out) there are, besides the thoracic fibrils—characterised by their extremely rapid contraction—in the wings of certain insects, other muscles, which are quite distinct anatomically and physiologically, and are of very inconsiderable bulk as compared with the others (the wing-muscles proper). The presence of two kinds of muscles is in obvious relation with two distinct actions. One of these is the unfolding of the wing-apparatus, arrangement of the wing-cases, and spreading of the wings. This action resembles the leg-movements. The second action, on the contrary, is that of actual flight, which has been shown by Marey to depend upon an extraordinary frequency of the beat of the wings in insects. In this case the anatomical difference between quick and sluggish fibres is very significant, and the thoracic fibrils are accordingly distinct on anatomical as well as physiological grounds. They comprise to a certain extent all those properties which are, as a rule, characteristic of muscles that contract permanently and quickly, *i.e.* great abundance of sarcoplasm, and a marked development of cross-striation.

The histological differences between quick and sluggish muscles are much less in the majority of cases. As a rule it may be said that *the latter, at least in vertebrates, are richer in sarcoplasm, dark, and often smaller; while the quick, excitable, more easily fatigued muscle-fibres contain less sarcoplasm, and are therefore clearer and usually broader.* As shown above, the dark fibres are often, though not invariably, stained by hæmoglobin and other colouring matters. This is very conspicuous in the Pecten family, where the greater (yellowish-gray) portion of the adductor muscle consists of striated, the (whitish) remainder of smooth, muscle-cells. As Coutance and Thoring showed, the former serves only the *rapid* closing of the shell, while the smooth muscle closes it *slowly*, but permanently and forcibly. This becomes impossible, and the shell gapes open, if the smooth part of the muscle is cut through; the striated part can still effect rapid closure on excitation, but never of long duration. The nicety of such an arrangement is obvious. Coutance (18), and later Knoll (17), showed the marked difference in the contraction process between the smooth and striated parts of the adductor muscle when directly excited. Lima inflata (according to Knoll) behaves like Pecten; its adductor muscle does not, indeed, consist of two macroscopically distinct portions, but it contains smooth elements in many layers at the periphery, and singly in the interior, while the bulk of the muscle is composed of cross- (or obliquely-) striated cells. When undisturbed in sea-water, the shells of these muscles usually gape open pretty widely, but from time to time they are sharply closed, and this movement, as in Pecten, jerks the animal a step farther. In the Oyster also the adductor muscle consists of two parts, one transparently gray, the other white and tendon-like; in Mytilus only the white, in Solen only the gray are present. Schwalbe, who was first to recognise that the gray part consisted of "bi-obliquely striated" muscle-cells, also pointed out the functional differences between the two portions. If the act of adduction is compared in the shell of Ostrea and Mytilus the first is seen to close sharply and suddenly with external excitation, the second very slowly and gradually, so that the adductor muscle can be divided while the shell is open, and the knife is not wedged in, as would happen in the oyster. Schwalbe therefore thinks that the bi-obliquely striated fibres of Ostrea serve for sharp,

energetic contractions, while the longitudinal fibrils in this case also produce permanent closure. In *Anodonta*, where a similar differentiation of the adductor muscle is shown in two sections visible to the naked eye, neither Engelmann nor Biedermann was able to detect any perceptible difference in rate of contraction between the differently coloured parts of the muscle (19).

II.—DEPENDENCE OF MUSCULAR CONTRACTION UPON STRENGTH OF EXCITATION

A systematic inquiry into this point is best effected with the aid of electrical excitation, in the form of single induction shocks, the strength of which can be graduated in the finest proportions. We are thus in a position to determine the law of dependence of contraction upon strength of excitation. It is easily proved that below a certain minimal limit of intensity (*the threshold of stimulation*) the excitation produces no visible effect; the discharge of a contraction begins first with a given strength of excitation, and its magnitude (height) increases for some time, according to Fick, in proportion with increased strength of stimulus. Beyond a certain point, however, the increase in contraction ceases, and the existing maximum is maintained for each increment of stimulation. This maximal limit is usually but little above that at which the first just perceptible contraction was yielded. The entire process of this greatest contraction and extension is known as a *maximal contraction*. It may be described in Fick's words (20) by saying, "Each impact of excitation discharges either a maximal contraction or no contraction at all; it is only in a limited interval of the scale of excitation (often hard to find on account of its narrow proportions) that *sub-maximal*, so to say, imperfect, contractions are given." We shall presently see that there are muscles (heart) which yield only maximal contractions.

The law of approximately proportional increase in height of contraction within the given narrow interval, deduced by Fick from experiments on indirect excitation of skeletal muscle, was subsequently disputed by Tigerstedt (21), who found (with direct excitation of curarised muscle also) "that with uniform increase of strength in the electrical stimulus, the muscular contractions

increase quickly at first, and then more and more slowly (probably in the form of a hyperbola), until they finally reach an asymptotic maximum" (*l.c.* p. 16), a proposition which Hermann had also put forward (4, p. 108). Cardiac muscle seems, as was said above, at first sight to differ from all the striated, skeletal muscles in its lack of correspondence between strength of excitation and magnitude of resulting contraction. It appears from Bowditch and Kronecker (22) that, under all conditions, induction currents of a given intensity produce maximal twitches of the previously resting muscles of the ventricle; weak stimuli produce no effect, while stronger stimuli elicit no more than the minimal effective stimulus; *minimal stimuli are therefore*, as Kronecker says, *at the same time maximal*, and even the most careful gradation of the stimulus fails in the heart to produce an incomplete contraction. There seems to be only one exception to this rule, under very special circumstances. Mays (23), *e.g.*, finds that occasionally in the apex of the frog's heart, with higher as well as with lower working capacity, the height of the pulse (twitch) will vary considerably with the strength of induction shocks sent in at a uniform rhythm. He obtains this result most certainly when the ventricle is filled with stale blood, and working in the oil-bath of the manometer.

For the rest we can but agree with Fick when he sees in these peculiarities of cardiac muscle "the extreme development of a property common to every other muscle-fibre," since here also "the breadth of interval in the scale of excitation for sub-maximal twitches stands in no relation to the unlimited portion of the same scale corresponding with the maximal contractions." This in no degree solves the problem of the latter, since it is difficult to see why, beyond a certain limit, any given strength of stimulus should only produce quantitatively equal responses, *which never correspond with the outside maximum of contraction*.

Apart from other facts to be discussed later, this is evident experimentally, since what is not produced by increment of excitation can be obtained by rhythmical repetition of uniform stimuli. The height of contraction, *i.e.*, may increase under given conditions, when uniform induction currents are sent into the muscle at uniform intervals. This striking effect was first observed by Bowditch, again in cardiac muscle, and confirmed by Tiegel and Minot in the skeletal muscle of the frog, Rossbach in warm-

blooded muscle, Richet in the muscles of crab, and Romanes in medusa (24). If uniform induction currents are sent rhythmically through the resting apex of the frog's heart, a ladder, or "staircase," of contractions with increasing amplitude is almost invariably exhibited, as shown in the accompanying series of curves (Fig. 37).

Tiegel (*l.c.* p. 37) observed an analogous effect in curarised

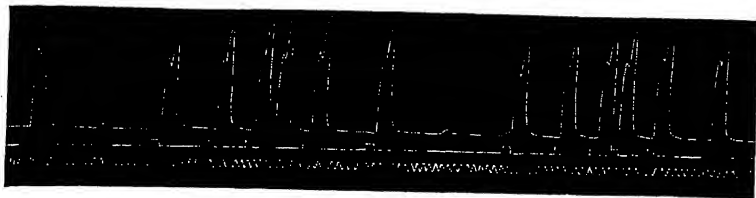


FIG. 37.—Heart (Frog) artificially excited after ligature of the sinus. The first notch of each curve is produced by the auricular, the proper summit by the ventricular systole. Both exhibit the staircase. (Engelmann.)

frog muscles (gastrocnemius) with intact circulation. If single induction shocks of uniform strength are sent into such a muscle at regular intervals, the height of contraction increases constantly, so long as maximal stimuli are employed, even in a series of several hundred contractions, so that the height of the "staircase" (*i.e.* the curve which unites the joint summits of an ascending series of contractions) increases within certain limits with

FIG. 38.—Excitation of a somewhat exhausted bloodless gastrocnemius of Frog, by groups of 1, 2, 3, 4, 5, uniform maximal break induction shocks. Increase in height of contraction with repeated excitation at short intervals ("staircase"). Decrease on longer duration of the pauses (tuning-fork, $\frac{1}{16}$ sec.) (Engelmann.)

the strength of the individual stimuli. On the application of minimal stimuli, there is, as a rule, no increment of the contraction series, or at most a trace only, whereas in the maximal series it is invariably well developed (Fig. 38). If such a series is interrupted and resumed after a pause, the first of the new contractions is smaller than the last before the interval (Tiegel, Rossbach, Buckmaster), but the muscle immediately resumes its increasing contractions. Within a certain range it is absolutely

indifferent at what interval the periodical excitations follow. A maximal limit is only given in order that the stimuli should not follow too slowly, if a "staircase" be required. This maximal limit is about 60 secs. for the cardiac muscle of the frog according to Bowditch, about 5 secs. for the striated skeletal muscles of warm-blooded animals according to Rossbach. The minimal limit is determined by that interval of stimulation at which the series of twitches fuses into a tetanus. In regard to the *form of the staircase*, it should be remarked that it is always, independent of strength and frequency of excitation, an equilateral hyperbola.

When it is remembered that this manifestation is independent of the nature of the stimulus (occurring equally with mechanical excitation), as well as of the volume of blood in the muscle, there can be no doubt that we are in presence of a process which is intimately connected with the excitatory process, or contraction, in the muscle. We must reserve for a later point of the discussion the probable cause of the above reaction, only remarking in conclusion that a similar, perhaps more permanent, after-effect to that following each single twitch, also appears after a tetanising excitation. Both Rossbach (*l.c.*) and Bohr (25) found that the same excitation produced a greater effect (stronger contraction) after than before the tetanus. With maximal stimuli this positive after-effect often continues for more than half an hour.

The latent period, as well as the height of muscular contraction, is partly dependent upon the strength of the excitation. Helmholtz's estimation of the latent period as 0.01 sec. with direct excitation of frog muscle (gastrocnemius) by single break induction shocks, has been proved far too large by later investigators; the variously estimated values of Place, Klünder, Lauterbach, Gad, Mendelssohn agree in showing that the latency period of frog's muscle, directly excited with induction shocks, is only from 0.005 to 0.006 sec. (cf. Tigerstedt, 26). Tigerstedt (*l.c.* p. 152) also obtained the same result from his own extensive observations. There is, moreover, the possibility that the latent period of muscular contraction is even less in value, since other significant data are included in the same computation. Burdon-Sanderson (27) calculates the latent period of frog's muscle at 0.0025 sec. only, and Regeczy (28) even denies its

existence. Helmholtz observed that in working with induction currents strong enough to produce the maximum of contraction, the intensity of current may be altered arbitrarily without in any way affecting the time-relations. Tigerstedt finds the latent period of contraction, with direct *maximal* stimulation from break induction shocks, to be independent of the strength of excitation in non-curarised as in curarised muscle. But within that range of current intensity, in which the height of contraction does increase with the increment of stimulation, the latent period, according to the same author, steadily increases with decreasing height of contraction, at first more slowly, subsequently in increasing proportions. This is true of normal, as well as of curarised, muscle.

The Latent Period of the Entire Muscle and of the Muscle Elements

At this point we must attack the question often raised in recent discussions, whether the latency period of the *muscle element* (*i.e.* smallest section of a primitive fibre) differs or no from that of the *entire* muscle (consisting of many fibres). All the observations, after Helmholtz, on the time-relations of contraction, refer to individual muscles in the coarse anatomical sense. But if we look more closely into the mechanical alteration in state of the muscle elements (*i.e.* least possible segments of a fibre) it is evident that not only the *active* changes in form and constitution, produced by the excitatory processes, but also the *passive* disposition, which results from the interconnection of the individual elements in the continuity of the fibre, must be taken into consideration. To a final theory of the muscular process the former only is of immediate importance, but the other factors cannot be neglected, since, as is easy to see, they are essentially significant in the mode of manifestation of the contraction of the entire muscle. It is not difficult to show that on exciting one end of a loaded muscle with parallel fibres, the part farthest from the point of excitation will submit to a considerable extension before it goes into contraction. This is best seen in polymerous muscles (29). If, *e.g.*, the rectus int. maj. of the frog, which has an oblique tendinous intersection towards the centre, is made to hang vertically with the tibial end upper-

most, and provided with two levers, one of which is inserted in the upper half of the muscle just above the intersection, the other in the cartilaginous acetabulum, and if the lower half of the muscle is then excited with single induction shocks, the graphic record of the change in form of both halves of the muscle shows at once that at the moment when the lower and directly excited half begins to shorten, the upper remains passively extended (Fig. 39).

"But the consequent rise of the upper curve soon changes into a fall below the abscissa, corresponding with a shortening of the upper half of the muscle," which is brought about *passively*

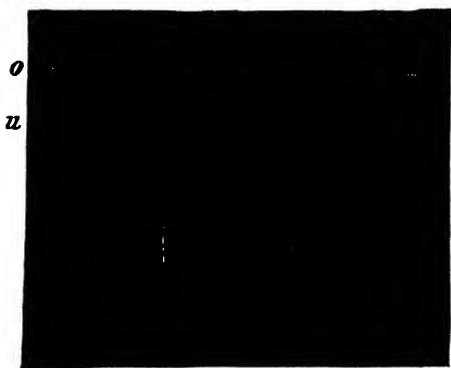


FIG. 39.—o, Upper; u, lower half of muscle. (Münzer.)

like the previous extension. "As soon as the lower muscle contracts, its two ends are drawn together, *i.e.* it raises the weight on the one side, and extends the upper half of the muscle on the other. But the weight, once set in motion, rises in virtue of its inertia far beyond the intrinsic height of lift ('height of projection'). At the same

moment the entire muscle, including the upper half, is unloaded; the latter flies back, and shortens, thus simulating a *natural* contraction" (*l.c.* 251).

This phenomenon was actually applied by Regeczy (30) in support of the view that the excitation process passes from one half of the muscle to the other by means of a tendinous intersection. If all jar is avoided, extension of the upper half of the muscle only will be produced under uniform conditions, persisting so long as the lower half remains contracted. What is here said of a polymurous muscle, divided by a tendinous intersection into two parts, physiologically independent of one another, applies equally to the two halves of a monomurous, parallel-fibred muscle, *e.g.* sartorius, the lower end of which is loaded and excited, a light lever being pushed through the centre of the muscle. The upper half of the vertically dependent muscle will always be

CHANGE OF FORM IN MUSCLE DURING ACTIVITY

perceptibly extended before it begins to shorten (31). This effect fails when the recording lever is connected with the lower end of the muscle, *i.e.* under normal conditions of recording a muscular contraction. The shortening of the *entire muscle* is not therefore preceded by any lengthening (extension). Each individual *muscle element* is, however, in the first place extended by the excitation, or contraction, of a distant spot, for the loaded muscle exerts a greater traction on its point of dependence so long as it pulls up its load in contracting, than during rest (Gad). It is therefore clear that under these conditions the mechanical latent period of the whole muscle must be longer than the mechanical latent period of the muscle element, and that accordingly the shortest latent period observed in the whole muscle must approximate most nearly to the true value of that of the muscle element. In order to cut out this delay in the latent period as far as possible, each point of the entire muscle would have to be simultaneously excited, which is not the case in any form of electrical excitation. Even where current passes through the entire muscle, the excitation, as will be shown, proceeds only from given points of the area stimulated. Here, again, the mechanical latent period represents only the upper limit of the true latency, since the energy (mechanical yield of work) of the muscle must already have exceeded a certain output, in order to produce a visible movement of the lever.

Tigerstedt (*l.c.*), from a great number of experiments, carried out under most varied conditions, determined the following values for the mechanical latent period in the frog's *gastrocnemius*:—

Latency Period in Secs.	Experiments.	Percentage.
0·003	1	1·2
0·004	19	22·1
0·005	35	40·7
0·006	24	27·9
0·007	6	6·9
0·008	1	1·2

According to this table the mechanical latency would be from 0·004 to 0·006 sec.; in most cases (41 %) it was 0·005 sec. The mechanical latent period of the *muscle elements* could certainly not exceed 0·004 sec., but is probably much smaller, since it is certain that within the time usually reckoned

as the latent period of muscular contraction, *i.e.* between the moment of excitation and the estimated commencement of contraction, a great number of muscle elements must already have been thrown into mechanical activity. Conclusions as to the latency of muscle elements might with more justice be deduced from the latent period of the *expansion* of a directly excited point of the muscle, by which the state of activity of any muscle particle can be followed as it develops. A muscle element is much too small to produce any perceptible mechanical effect by itself in contracting, so that the question of the magnitude of its mechanical latent period cannot be solved by direct experiment (Gad). It may be taken as proved by experiments, which we shall discuss later, that there is no latency period in the *chemical changes* in muscle substance, consequent upon excitation; whether there is any appreciable interval before *mechanical energy* is locally developed, must be regarded as questionable.

III.—EFFECT OF LOADING (TENSION) UPON MAGNITUDE, DURATION AND FORM OF MUSCULAR CONTRACTION

It has been shown that the absolutely unloaded muscle (*e.g.* swimming in mercury) retains its contracted form if no extending force is acting upon it. It is therefore impossible to obtain a graphic record of the process of shortening and elongation in a perfectly unstretched muscle. Some kind of lever, however light, must rest upon it, and the movements of the lever are counter-balanced by a traction (load) working against the shortening, as soon as relaxation commences. This entails certain errors in the curve of the contraction which—particularly in the older experiments, where inert masses were not eliminated—have been a great source of confusion. More especially in the descending portion of the curve, secondary smaller waves, with no corresponding active changes of form in the muscle, are produced by intrinsic variations of the rapidly accelerated falling mass. At a later period these fallacies were almost wholly avoided by using the lightest possible lever, and choosing a suitable point of attachment for the load (20). Where the tension of the muscle remains approximately constant during the course of a contraction—as is the case when it is attached to a long one-armed lever, of the smallest possible bulk, while a weight close to the

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fulcrum pulls on the same lever in the opposite direction—such a contraction is termed “isotonic” (Fick) (Fig. 40). It will then be found as a rule that, with heavy loading, the height of such contractions decreases gradually with the magnitude of the constant tension, rapidly at first, and afterwards much more slowly, but by no means in proportion with the loading, so that the corresponding yield of work increases simultaneously without interruption (cf. Santesson's tables, *Scandinavischen Archiv*, i. 1889, p. 25 f.) Under certain conditions a direct increase in magnitude of contraction (height of twitch) is visible with increasing tension. As early as 1863, A. Fick observed in the adductor

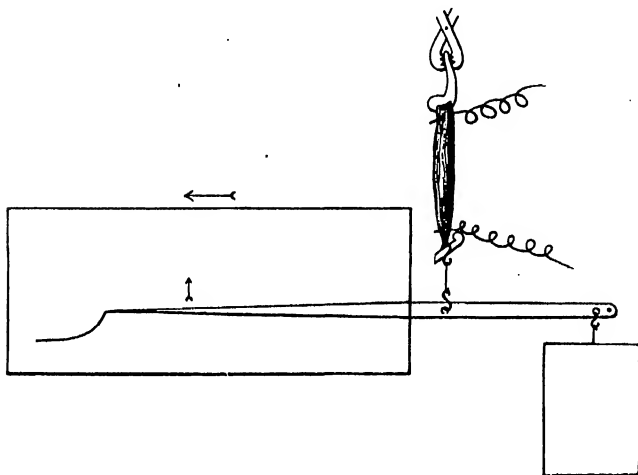


FIG. 40.—Isotonic Method. (Gad.)

muscle of Anodonta, which consists of uninuclear fibre-cells, that the height of lift increased with increase of loading; Heidenhain asserted the same paradoxical fact in tetanising striated frog muscle, and later on it was also determined for single twitches by different experimenters, provided that during the isotonic process the load is not excessive (Fick, Marey, v. Frey, 32). More especially in the case where the tension of the muscle in contraction increases constantly, or from a given moment (e.g. when the muscle pulls on an elastic spring), the shortening will be greater with stronger, than with diminished, initial tension. This fact was indeed established by Fick when he showed that if a muscle is appropriately hindered in shortening, and the

time between stimulus and discharge of the muscle judiciously determined, the twitch is invariably greater than under normal conditions. The same also appears when the muscle is loaded with increasing weights, and discharged at the same moment after excitation. Place (32) found that on using a spring lever where the resistance to be overcome, and consequently the tension during the course of a contraction, increases steadily, the height of the twitch increases also if the initial tension is raised from 0 to 25 gr. Tigerstedt (26) subsequently observed an increment in height of contraction with even higher initial tension, under similar conditions; and, lastly, the same relation is treated very circumstantially by C. G. Santesson (32).

From all these experiments we may conclude that within certain limits the magnitude of contraction (height of twitch) increases along with the initial tension, as well as with augmentation of tension, during the period of contraction, to which it must be added that this increment in height of twitch can neither be due to the mechanical conditions of the experiment, nor to any temporary alteration of excitability from the electrical stimulus, but must be referred to a specific property of living muscle-substance. As Fick expressed it, the muscle is not at a given moment of the twitch invariably the same elastic body possessing a given (uniform) tension in virtue of its actual length at the moment. The cause of these manifestations can rightly be looked for in nothing else than in a latent state of excitation, produced by, and varying with, the mechanical conditions under which the twitch is consummated. Schenk (33), indeed, states boldly that the strong reaction by which the muscle always responds when its contraction is in any way inhibited or even hindered, reacts upon it again as a "stimulus," which may in its turn affect the processes both of contraction, and, under some conditions, of resolution of contraction also. As a rule the *duration* of the contraction alters simultaneously with the height, on increasing tension of the muscle; on the other hand, the commencement of shortening is not visibly affected. On raising the equilibrated mass to be moved by the muscle to 200 grs., Tigerstedt found that the latent period was very slightly lengthened in comparison with its proportions when only a light lever of hardly any bulk was carried.

The reaction thus described for the striated skeletal muscles of

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Vertebrates is by no means confined to them, but occurs even more demonstrably in smooth, as well as in cardiac, muscle. We have already referred to Fick's experiment of the effect of increased tension from increased loading on the magnitude of contraction in the adductor muscle of Anodonta. The consequences of augmented tension on cardiac muscle are very striking, both in vertebrates and invertebrates. The effects observed are indeed somewhat ambiguous, owing to the intracardiac nerves, which, as a rule, govern the normal rhythmical movements of the heart, and whose interference is not easily excluded. The simplest experiments are those with the a-ganglionic ventricle of the frog's heart, which has been separated from the auricle—the so-called *apex*,—or with the snail's heart (*Helix pomatia*), where no ganglion-cells have positively been discovered. Since the apex of the heart—like all excised skeletal muscle—contracts only on artificial stimulation, otherwise remaining permanently quiescent, it is admirably adapted to experiments on the effect of increased tension of the muscle-wall, from increase of intracardiac pressure on excitability and work yielded. These experiments were first introduced by Ludwig and Luchsinger (34). In order to isolate the pressure effect as far as possible, the apex of the heart was filled with physiological salt solution. Regular rhythmical pulsations of a ventricle, which had previously been quiescent, will usually begin at a pressure of 20–50 cm. of water. A small mechanical stimulus is usually required to bring about the first contraction, which is then followed spontaneously by an entire series. The pulsation varies regularly with change of pressure, and is indeed higher within a certain range, in proportion with the pressure (cf. tables of Luchsinger, *l.c.* 293). Engelmann (35) made similar observations on the equally a-ganglionic bulbus aortæ of the frog. The effect of tension of the wall is, however, seen most effectively in the thin-walled snail's heart (36). Even in the living animal, it may be seen that evacuation of the quiescent heart, by snipping it, produces a more or less prolonged pause in diastole, or a much retarded action. If the heart is excised it is evident that every expansion of the relaxed and empty ventricle, however slight, is sufficient either to set up (rhythmical) contraction or to accelerate the beat considerably, so that the force of the individual contractions also must be essentially augmented. The same fact has also been established by Schoenlein (37) for the heart of Aplysia. When the extension is not too weak, and in

particular where it lasts for a considerable period, a more or less extensive *after-effect* may regularly be observed—the rhythmical contractions even lasting for some time after tension is removed from the heart. Ludwig and Luchsinger observed the same after-effect on the frog's heart.

In *Helix pomatia* it is easy to introduce a convenient canula through the auricle into the upper part of the ventricle, and so fill the heart with fluid (snail's blood). Under these conditions, the internal pressure, together with the amount of wall-tension, undergoes the simplest alteration. It is often sufficient to incline the charged canula, with the heart, a little out of the horizontal, apex downwards, in order to produce pulsations in the previously quiescent ventricle. Another method, which is in many ways more convenient, is to place the canula vertically with the heart, so that the pressure of the entire column of fluid acts on the inner wall of the ventricle. It is then easy by gradual immersion in a second vessel, filled with 0.5 % salt solution, to raise the pressure acting upon the external surface of the heart from zero to the point at which internal and external pressure are equal, and wall-tension therefore abolished. The difference of level of the fluid in the tube and in the external vessels will then be the measure of amplitude of wall-tension at any moment. The following figures illustrate the changes of pulse-rate with change of wall-tension under the above conditions:—

Height of Pressure, (Difference of Level in Canula and External Vessel.)	Beats per minute.
30 mm.	50
15 "	36
8 "	21
5 "	11
2 "	0
30 "	50

Luchsinger (28) has also been able to show in the rabbit's ureter the effect in this smooth, muscular organ, of wall-tension on contraction phenomena; so that in view of all the previous evidence we cannot doubt that increased tension increases the yield of work, not merely in striated skeletal muscle, but in an even higher degree in the heart and smooth muscles. And this increase is expressed not only in an increment of the individual contractions, but also in the discharge or acceleration of rhythmically repeated contractions, i.e. the augmented (wall-) tension

does not merely increase the excitability, but it also acts directly as a discharging stimulus. Heidenhain showed for striated skeletal muscle that not merely the mechanical yield of work (which is essentially conditioned by the magnitude of contraction or height of twitch) increases, but that, generally speaking, a larger proportion of the potential energy stored up in the muscle is employed, *i.e.* that exchange takes place between the greater part of the chemical tensions; and this has been confirmed by later experiments. But when this occurs with one and the same strength of a given stimulus, the cause must lie in a change of state in the muscle itself, which might be termed increase of excitability. When we find that, beyond a certain point, expansion, or tension, *per se* may act on cardiac muscle as a permanent stimulus, inasmuch as without the addition of any further stimulus it can discharge long series of rhythmical contractions—while in other cases an external impact, a new stimulus, may also be required, which, however, would be inadequate without the simultaneous extension of the muscle—it seems legitimate to refer *the increase of excitability* (of which it is usual to speak in the latter case) *to the presence of a permanent condition of excitation, caused by the extension-stimulus, but in itself inadequate to produce visible effects of stimulation.* From this point of view the state of increased excitability of living matter would only gradually become distinguishable from the state of excitation. Later on we shall encounter numerous facts which are in favour of this theory.

When a muscle is so heavily loaded that it is unable to raise the suspended weight, the most powerful stimulus will fail to produce any external *visible* alteration, while at the same time the properties of the muscle are fundamentally altered. In the first place, the elastic traction (tension) of the excited muscle is considerably greater in its initial length (*i.e.* in its unexcited state) than it is in the resting condition, for the true contraction first appears in consequence of this altered state, since the dependent load is overcome by the increase of elasticity due to excitation. By using Fick's method it is possible to prevent a muscle from perceptibly altering in length, and at the same time to show its actual tension by a visible indication. This is most simply effected by attaching the muscle to the short arm of a two-armed lever, while an elastic spring confines the movements of the longer arm. If the latter is drawn out beyond the point of insertion of the spring,

and allowed by means of a writing-point to record its movements on a travelling surface, a curve will be obtained (with almost total exclusion of change of form in the muscle) which represents

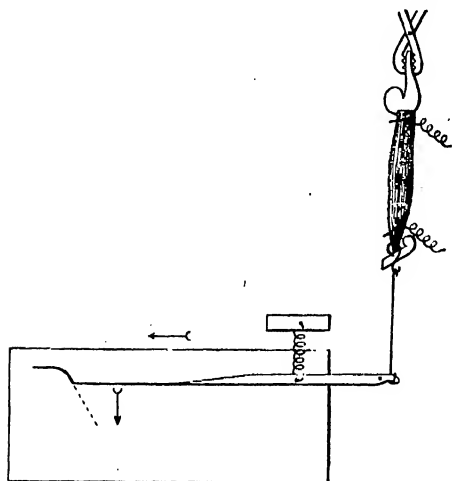


FIG. 41.—Isometric Method. (Gad.)

essentially the increase and decrease of tension during contraction, with approximately constant length of muscle (Figs. 41 and 42). Such a curve is termed by Fick an "isometric" curve of contraction, because it is recorded with uniform length of muscle, while with the usual "isotonic" method, on the contrary, the tension remains approximately constant, and the muscle contracts freely. It is

naturally impossible to obtain a tracing of an absolutely isometrical muscular contraction; for if a lever is to be moved, and serve as index of increasing and decreasing tension, the muscle cannot be stretched quite immovably between two points, as would be required in absolutely mathematical and exact isometry. The force opposing the tension is rather exercised by a movable body, which draws a writing-point nearer or farther, according to the magnitude of the tension.

Yet this occurs in so slight a degree with Fick's tension-indicator that the highest appreciable tension-value in the shortening of the muscle is only a fraction of a millimeter. The tension-values to which a muscle attains its contraction are under some conditions very considerable. If isotonic be compared with isometric curves, described by the same muscle under uniform conditions, we find invariably

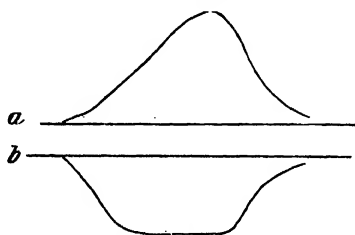


FIG. 42.—a, Isotonic curve of twitch; b, isometric curve of twitch.

that the summit of the latter lies much nearer to the initial point than the summit of the isotonic curve, i.e. in other words, with constant length the muscle reaches the maximum of tension much sooner than with constant tension it reaches the maximum of shortening (Fig. 42).

IV.—EFFECT OF FATIGUE UPON THE PROCESS OF MUSCULAR CONTRACTION

The most fundamental sign of distinction between living and dead matter is undoubtedly that of Metabolism, i.e. chemical processes taking place within the living matter. By these certain substances are produced, on the one hand, which are finally excreted as useless to the organism, while, on the other, nutritive substances are taken up and assimilated. With Hering we may call the former process "dissimilation," the latter "assimilation." Hering's conclusions as to these two fundamental processes of metabolism are so important to our subject as to demand a full exposition, and this is best given in his own words (40). "Assimilation and dissimilation must be conceived as two closely interwoven processes, which constitute the metabolism (unknown to us in its intrinsic nature) of the living substance, and are present simultaneously in its smallest particles, since living matter is neither permanent nor quiescent, but ever more or less in constant motion. It is a fundamental property of living matter, engrained deeply in its nature, to assimilate and dissimilate; and these processes continue, provided only the essential conditions of life are present, without assistance from external stimuli." In so far as living matter is wholly unaffected by the occasionally working external stimuli, Hering designates its assimilation (A) and dissimilation (D) as "autonomous."

"So long as the autonomous D and A are equal in ratio, the state of living matter cannot be altered, and it remains the same qualitatively and quantitatively." This state of perfect equilibrium between the autonomous D and A is termed by Hering "autonomous equilibrium."

"This condition of living matter is altered when any stimulus incites it to active dissimilation, which is not balanced by equal assimilation. Under these conditions D is no longer exclusively autonomous, but is reinforced by outside factors; it may there-

fore be denoted as *allonomous*, in distinction from the purely autonomous process. The increased formation of D-products, and corresponding loss of elements which were formerly an integral part of the living matter itself, and entered into its chemical composition, produces intrinsic alteration in the substance in proportion with the strength and duration of the stimulus. Hence at the close of excitation the substance is found to be quantitatively and qualitatively altered."

If the D-process is regarded as a function of living matter, it must at this stage be designated as *less capable of functioning*. Since the substance is altered, not merely qualitatively but quantitatively also, its state, after the action of a D-stimulus, as compared with its earlier condition, may in Hering's terms be denoted as "below par"; obviously, therefore, as soon as the D-stimulus begins to act, the depreciation of the living matter proceeds *pari passu*, increasing with the duration of the excitation. The potential dissimilation of the substance, however, diminishes in the same ratio.

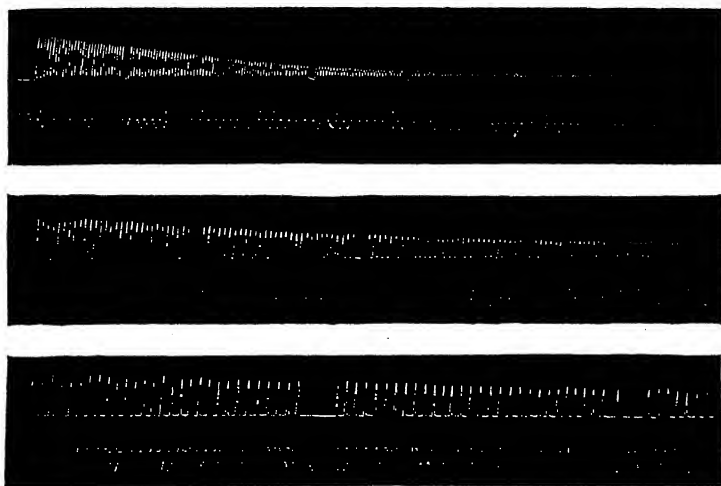
This accordingly denotes that excitability diminishes in proportion with the duration of the D-stimulus, or, as it is usually expressed, the substance *fatigues* itself. This indisputable action of every D-stimulus may be further reinforced in its physiological effect by an aggregation of disintegration, or dissimilation, products, which, beyond a certain limit, are in many cases demonstrably inimical to the functions of the living matter.

The manifestations and laws of "fatigue" were first investigated in cold-blooded muscle (excised, or *in situ*) by Kronecker (41) and Tiegel (24); in warm-blooded muscle by Rossbach (24); and, recently, in man by Mosso (42). A number of conclusions have been reached, some at least of which must be quoted.

Muscular fatigue is indicated experimentally by the greater strength of stimulation required in order to produce a constant yield of work, *i.e.* same height of lift in contraction as in the unfatigued state, or, conversely, by the decrease of lift, or yield of work, with constant stimulation. If the muscle is excited rhythmically—at constant intervals, with uniform *maximal* stimuli and resistance—by single induction shocks, a double alteration of the contraction curve is seen in height and in duration. Kronecker found in frog muscle that the lift diminishes regularly from twitch to twitch, and that by a constant fraction of de-

crement. The *curve of fatigue*, i.e. the line connecting the

A



B

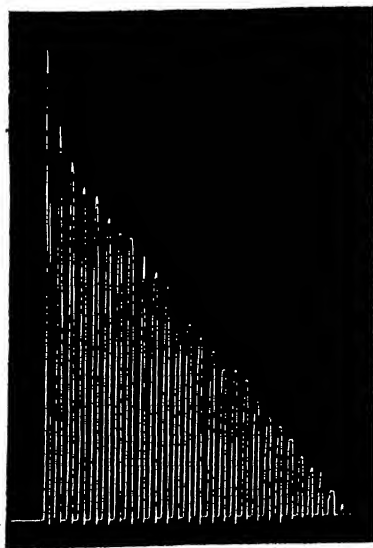


FIG. 43.—A, Twitches of a non-curarised Frog's gastrocnemius with normal circulation. To show acceleration of fatigue with increased frequency of stimulation. Tuning-fork, $\frac{1}{10}$ sec. (Engelmann.) B, Series of contractions of flexor muscles of finger, artificially excited. The load (1 mgr.) was carried till the finger became exhausted. (Mosso.)

tops of the single twitches (recorded at equal distances upon a stationary surface), is in this case a *straight line* (Fig. 43, *A* and *B*) with direct excitation of the muscle.

Excised muscle becomes exhausted after a certain number of twitches. According to Tiegel, the same thing occurs in curarised muscle that has been freed from blood, on rhythmical excitation with *sub-maximal* induction currents. The first (20 to 30) twitches of a series are the only exception to the rule that the extreme upper point of equidistant contractions lies in a straight line; in these the curve, instead of falling, rises in a staircase (*supra*). In the case of curarised muscle with normal circulation, this rise may extend over several hundred twitches, of which over a thousand may remain at the same magnitude, while the rest sink slowly but continuously (Tiegel). Accordingly, as might be presumed, fatigue proceeds much more slowly in muscle with normal circulation and nutrition than in excised bloodless preparations, and the period of "staircase" increment in the twitches is much shorter in the second than in the first case. It is remarkable that, according to Tiegel (*l.c.* p. 18), the curve of fatigue (*i.e.* straight line) sinks much more rapidly to the abscissa (*i.e.* makes a greater angle with it) with sub-maximal than with maximal stimuli; *i.e.* the muscle is more quickly fatigued by sub-maximal than by maximal excitation, provided the two kinds of stimulus alternate regularly at short intervals. When a muscle has yielded a series of twitches at maximal, or sub-maximal, excitation, and the rhythm is changed to a weaker stimulus, returning immediately (after twenty or more twitches) to the original excitation, the first contractions of the last series are invariably higher than the last of the first series (Tiegel). The muscle apparently recovers during sub-maximal excitation from the stronger (maximal or sub-maximal) stimuli. The height of twitch diminishes more rapidly in proportion as the excitation interval is shorter (Fig. 43, *A*), and this law holds both for maximal and sub-maximal stimuli in curarised muscle. In muscle with normal circulation and nutrition, there is always an interval between each pair of stimuli, in which the height of twitch does not diminish even after protracted excitation, and no fatigue appears (*e.g.* the beating heart). Hence we may assume, from the previous observation, that during each pause in stimulation the "down" change caused by each D-stimulus in the

muscle-substance is completely compensated by the A-process. In other cases (with greater stimulation-frequency), it is perfectly intelligible that a progressive fatigue and decrement of the magnitude of contraction must ensue. The only point that is difficult to elucidate is the initial staircase increment of the twitches, more especially in excised, bloodless muscle, which seems in direct contradiction with the previous theory. It is clear that we could only come to a right understanding of this phenomenon if the A-process, the invariable concomitant of the D-process, were more taken into account than has been customary in physiology. There are countless instances in which we may observe that living matter after undergoing the "down" change consequent on a D-stimulus, *i.e.* falling *below par*, returns from this state to the earlier *at par* of autonomous equilibrium, which "recovery" (due to preponderance of A over D) proceeds with so much the greater energy in proportion as the magnitude of the "down" change, caused by the preceding stimulus, has been greater.

It is possible that we have in this the interpretation of the fact mentioned above, that muscle fatigues more slowly with maximal than with sub-maximal rhythmical excitation. In any case, the living matter alters after each cessation of a D-stimulus in virtue of its inherent energy, in a sense inverse to its action during the stimulus, *i.e.* in an "ascending" direction. The "recovery" of such living substance, "fatigued" by excitation, is always an "autonomous ascending alteration," by which the depreciation of matter is compensated, and it is brought back to *par*, as previous to excitation.

It would further appear that, under favourable conditions, the "down" change of substance produced by a D-stimulus is followed by such an energetic "up" change that the much accentuated A-process becomes not merely *at*, but *above, par*—when it is of course succeeded by an augmented D-excitability. Such a rhythmical series would denote, not that the living substance (*e.g.* cardiac muscle) in equilibrium, alternated regularly in "up" and "down" changes between D and A, when the preceding "down" change would be completely compensated during the period of the "up" change,—nor that there was a "down" change in the value of the substance ("fatigue"),—but, on the contrary, that there was an *ascending alteration*, as expressed in increase of capacity for work and augmentation of height of twitch in the

muscle. From this point of view we are able satisfactorily to explain all the preceding evidence *re* staircase rise of contractions, and to see in it solely the expression of a general law, according to which not only the physiological capacity for work in any organ (particularly in muscle), but also its morphological development, which to the last degree is dependent upon nutrition, are conspicuously promoted by regular activity (effect of practice). The degeneration of muscles which from any cause have for a long time been inactive in the body, the pronounced development of the same when in vigorous exercise, afford sufficient proof of the favourable effect of muscular activity upon nutrition. This last is mainly subserved by *the regulation of the supply of arterial blood*, as exhibited in vertebrate muscles, which must also, of course, to a greater or less degree control the fatigue effects. Ludwig and Sczelkow observed in 1861 that the blood-vessels of muscles widened in contraction, so that the blood circulates through them more rapidly, and Tiegel (*l.c.* p. 81) found the same vascular effect in direct excitation of curarised frog's muscle. Such a muscle treated at regular intervals with maximal or sub-maximal stimuli (induction currents) grows more and more red in the course of excitation, and may even set up extravasulation. The long continuance of the "staircase" rise in height of twitch under these conditions must certainly be referred partly to this hyperæmia; but we have already pointed out that this is not its *sole* cause, as is self-evident from its appearance in bloodless preparations.

The effect of fatigue is, as we have stated, not merely to alter the height of the contraction as described, but also its time-relations, which with progressive fatigue become more and more extended. This retardation of the course of the twitch, which increases gradually during a long series of contractions, and expresses itself more particularly by a considerable extension of the phase of relaxation of the muscles, may finally attain such proportions that even with longer intervals of stimulation lasting for several seconds, the muscle has not time to relax to its original length before the beginning of the next contraction, and thus the base points of each individual curve rise higher and higher above the abscissa. Funke (43) has recorded cases in which the myogram at the later stages of fatigue resembled a steady tetanus curve, although the stimulation intervals lasted

several seconds. But the curve of contraction in fatigued muscle is not merely characterised by greater or less extension; its form also is modified, especially in the descending portion. Generally speaking, this change may be defined, with Funke, by saying that the descending portion of the curve gradually loses its character of a free fall, owing to the resistance engendered by fatigue and increasing with it, on which the lengthening of the muscle is more and more retarded, and always in earlier stages, by the weight raised by its own gravity. In the end, as Funke has aptly expressed it, the muscle resembles a viscous, doughy mass, responding with the utmost inertia to the traction which endeavours to bring it back to its original dimensions. The ascending portion of the curve, on the other hand, loses little of its steepness, even when fatigue is carried to exhaustion. The shorter the intervals between the single twitches, the more rapid will be not merely the diminution in contraction magnitude, but also the extension and change of form in the curve as described above. In individual cases, the stage of relaxation in otherwise normal, non-fatigued, striated muscle is conspicuously lengthened, so that, as first described by Kronecker (44) and subsequently investigated by Tiegel (45), the muscles may remain considerably shortened during long pauses (up to 10 sec.) in a rhythmical series of simple induction shocks. It is evident that this phenomenon, which Tiegel terms "contracture," can have nothing to do with fatigue, since with increased function of the muscle it diminishes instead of increasing. In this condition, which, as Tiegel found, is only developed in *direct* muscular excitation, the excitability of the muscle to normal stimulation *via* nerve is minimal, while the contracture may correspond with the height of the twitch. The muscles of spring-frogs seem especially prone to contracture, which then appears even with unimpaired circulation, and is the more marked in proportion with the intensity of excitation (cf. also Mosso, *l.c.*)

The course and process of the manifestations of fatigue must obviously be in the highest degree susceptible to all those data on which depend the assimilation, or dissimilation, of muscle-substance. Here, in the first place, we must consider *the original physiological condition* in which the muscle begins its fatigue-task, the widely varying range of its "capacity for work" and "excitability" in normal connection with the organism, or after

separation from it. We learn from experiment that every muscle which is excised and therefore deprived of normal conditions of nutrition, will sooner or later lose its excitability and become moribund. The interval at which this occurs is very unequal in different animals, even in the muscles of the same animal it varies considerably with external conditions. In any case we must assume that the autonomous equilibrium of the muscle-substance is permanently disturbed from the moment of its separation from the organism, since, in consequence of the less favourable conditions of assimilation with prolonged dissimilation, a constantly increasing autonomous "down" change ensues, as expressed in diminished excitability. As a general rule, we find that the muscles of cold-blooded animals preserve their excitability longer than those of warm-blooded animals, in consequence of their lower intensity of metabolism; yet this law is by no means universal. The muscles of fishes, for instance, seem to lose their excitability very quickly when separated from the organism (46). The expression "cold-blooded" further includes the Invertebrates, many of which (*e.g.* insects) possess muscles that perish very rapidly. It is noticeable that the muscles of the same animal do not all become moribund and lose their excitability with equal rapidity. If the sarcoplasm really possesses a nutritive function, as was shown above to be very probable, we might expect that the sarcoplasmic dark muscles would, as a rule, be fatigued and die less quickly than the a-sarcoplasmic clear muscles. According to Grützner's observations this actually is the case. Ranvier observed long ago in the triceps humeri of rabbit, which consists of pale (clear) and red (dark) fibres, that it responds at first like a pale muscle owing to the lesser excitability of the white fibres, but when fatigued with prolonged excitation it contracts like a red muscle, because the white portion is fatigued, while the red is still capable of serving. This difference also comes out very clearly in the fact that, according to Bierfreund (47), pale muscle falls into *rigor mortis* much more quickly than red muscle. Under the same conditions the first becomes rigid in 1–3 hours, the latter only in 11–15 hours after death. And when the rigor of the pale muscles has already passed off again completely (10–14 hours after death), the red muscles have not begun to lose their rigidity.

Finally, we have the observations of Rollett (48) on the very different contraction curves exhibited by *Dytiscus* and *Hydrophilus*. The fresh muscle of *Dytiscus* far exceeds that of *Hydrophilus* in regard to rapidity and energy of single twitches, but with prolonged activity the energy of its contractions soon gives way, and this is in a much more marked degree than their rapidity, although the latter also diminishes considerably. The more sluggishly contracting *Hydrophilus* muscle, on the other hand, maintains its energetic twitches at a comparatively high level, even after prolonged activity; in the process of fatigue, however, they become more and more extended, so that their duration may finally last twenty times longer than the contraction of fresh muscle.

As was said above, the muscle-fibres of the heart are distinguished by abundance of sarcoplasm, which may well be connected with their extraordinary vitality in many cases. Panum observed rudimentary pulsations of the heart in rabbit up to $15\frac{1}{2}$ hours, Vulpian in the mouse to 46, in the dog to 96 hours, after death (!). Single fibres of the cardiac muscle of mammals examined in physiological salt solution will often exhibit unmistakable rhythmical pulsations the day after death (Sigm. Mayer).

In all these cases, *temperature* exerts the greatest influence upon the total duration of existence, or the steepness of decline of excitability, both in isolated muscle and in the still living animal. This is intelligible when we remember the great significance of temperature for the intensity of all processes of metabolism, and, in particular, for that of autonomous dissimilation. We should therefore expect *a priori* that the death and corresponding decline of excitability would, as a rule, occur more rapidly with high than with low temperature. The effect of temperature is more positively marked in cold than warm-blooded animals.

Du Bois-Reymond has found gastrocnemius and triceps muscles of frog that were still excitable at 0° C. ten days after excision, while on a hot summer day excitability will disappear after 24 hours, and with medium temperature at about the third day. The data in this respect are insufficient in regard to skeletal muscle in warm-blooded animals. On the other hand, there are interesting observations on mammals as to the extraordinary re-

tardation of death by previous protracted cooling (artificial cold-bloodedness), which can be produced either by dividing the spinal column high up (Bernard), or by irrigating the skin of the belly with cold salt solution. In rabbits cooled in this way to 20° C. in 6–10 hours, the direct muscular excitability persists for 6–8 hours after death (Israel, 49).

There can be no doubt that the immediate cause of death in excised muscle is the interruption of the nutritive stream, and of the circulating blood in particular. Even in the living animal, interruption of circulation in a muscle, or group of muscles, produces paralysis in a short time, and eventually rigor. This experiment is only partially successful in cold-blooded animals, because their muscles, *e.g.* in Amphibia, though also dependent on the circulation, exhibit the effects of anæmia at a relatively much later period (Kühne, 50). The muscles of frogs are known to remain excitable for days, when all the blood has been driven out by injecting the vessels with 0.6 % salt solution (salt frogs). On the other hand, the striated muscles of warm-blooded animals, especially of birds, are correspondingly more sensitive, losing their excitability after a comparatively short time, and finally becoming rigid (Schiffer, 51) when the circulation is completely interrupted. It is, however, possible to restore or preserve excitability, when reduced or abolished by anæmia, by artificial transfusion of arterial blood. The time up to which this will succeed after loss of excitability is longer in proportion to its normal persistence (Brown-Sequard, 46). The excitability of smooth muscles in warm-blooded animals is much less dependent upon the circulation, and they are in this respect more like the striated muscles of cold-blooded animals.

Many unjustifiable assertions have been made with regard to the rapidity of death in smooth warm-blooded muscles, and their sensibility to alterations of metabolism, because the spontaneous movements of certain smooth muscular organs (*e.g.* intestine) cease very soon after death, and along with them excitability to artificial stimuli. But it may easily be shown that this seemingly permanent loss of excitability is really only produced *by cooling*, and that the sensibility to stimulation makes its appearance again when the temperature is raised artificially (Biedermann, 52). The muscular wall of the excised intestine of mammals retains its vitality in a most surprising

manner, and has been found excitable even more than 12 hours after death. So, too, the ureter of the rabbit or guinea-pig will, even after long immersion in cold, physiological salt solution, or when taken from an animal some hours after death (no trace of excitation being left under natural condition), become once more fully excitable if warmed to the body temperature (*loc. cit.* 387). A similar tenacity of life was found by Grünhagen and his pupils in the sphincter iridis of different mammals (53). Yet more resistant, according to Sertoli (54), are the equally smooth retractor penis muscles of certain mammals (horse, ass, dog), in which excitability continues for as much as *seven days* after extirpation. During the greater part of this time the muscle was in a temperature of 5° – 8° C., and at the time of the experiment was only warmed to 30° – 37° C. If the temperature remains at uniform height (39° – 40°) the excitability disappears in a short time.

The rapid fatigue of certain smooth muscles under perfectly normal conditions is in striking contrast with this great capacity of resistance to ordinary nutritive influences. Engelmann (*Pflüger's Arch.* vol. ii. p. 263 f.) pointed out the effect of fatigue in the rabbit's ureter after every individual contraction, mechanical excitability being *nil* immediately after each twitch has completed itself. During the subsequent pause it is gradually recovered. In a warm, fresh rabbit's ureter, where the blood is still normally circulating, the initial height of excitability is recovered after a few seconds. In the rat even one second is not required under the same favourable conditions. In cooled ureter, withdrawn from circulation, excitability returns much more slowly and imperfectly after contraction (5, 10, or more secs.)

Thus we see that excised muscles of cold-blooded (invertebrate and poikilothermic) animals usually become fatigued, and die, more slowly than those of warm-blooded animals; yet this is by no means an invariable rule, for, on the one hand, there are muscles of cold-blooded animals which lose their excitability quickly even at a low temperature (fishes, insects), while, on the other, certain smooth muscles of the warm-blooded animals remain excitable at low temperature for an extraordinary length of time, even when fully deprived of circulation.

The muscular fatigue consequent upon excitation is, as already

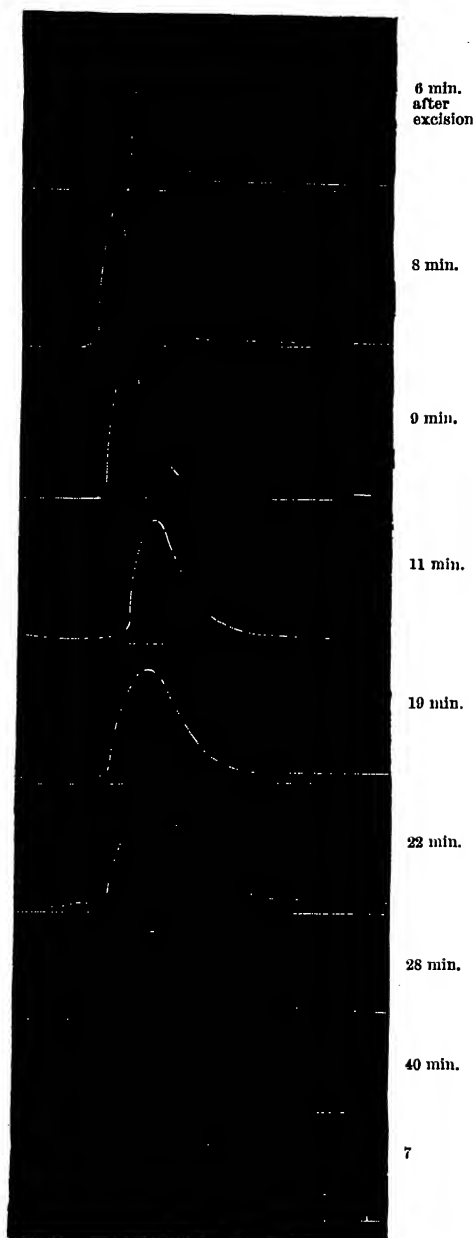


FIG. 44.—Contractions of excised Rabbit's heart.
(Waller and Reid.)

indicated, as much the effect of a "down" change in living matter, caused by the preponderance of D over A processes, as is the gradual death of a muscle separated from the organism, or deprived of circulation. We should therefore expect the changes which occur in the twitch (or contraction) in both cases to agree in all essential points. Decrease in magnitude of contraction (height of twitch), and elongation (extension) of the curve, appear in either case as distinctive features. This is very apparent in the pulsations of the excised mammalian heart (55), when the fall of temperature (*infra*) plays an important part (Fig. 44).

Although the condition of muscular fatigue may thus be referred mainly to a preponderance of the D-process over the simultaneously occurring A-process, *i.e.* to a diminution of the store of decomposable matters, or of chemical tension, we must not neglect the other and important factor which

Ranke in particular has pointed out, *i.e.* the accumulation of certain disintegration products (56).

Any considerable aggregation of the so-called D-products in muscle can only occur in preparations that are excised and withdrawn from circulation, and the rapid appearance of fatigue in such a muscle must at least in part be due to this factor also. The restorative effect of transfusion with (arterial) blood can only, however, consist in a minor degree in the elimination of the D-products (CO_2 , lactic acid, KH_2PO_4 , etc.), for otherwise a washing-out of the muscle with any indifferent fluid (*e.g.* physiological salt solution) would have the same effect as the infusion of blood, which never is the case.

Unquestionably, therefore, the blood carries to the exhausted or dying muscle, matters which are essential to the restoration of its working powers. With regard to the necessary *quality* of the blood, we can speak with certainty of a few elements only—oxygen, *e.g.*, which is indispensable to the maintenance of excitability and capacity of movement in *all* living substance.

Owing to the relatively large bulk of an excised cold-blooded muscle it is capable of little, or hardly any, physiological exchange with the atmosphere, which is only possible on the surface, and accordingly the presence or absence of free oxygen in the neighbourhood of such a muscle exercises a negligible influence upon the conservation or restoration of its excitability. In fact, Hermann (4, p. 132) finds that frog's muscle retains its excitability in perfectly indifferent gases (N, H), and still more *in vacuo*, as long as, or longer than, it does in the air. The transfusion of nutritive fluids containing oxygen, on the other hand, produces a very different effect. In this case a lively exchange of gases goes on between the blood, which circulates freely inside the muscle, and the muscle-substance, and here the beneficial effect of oxygen on excitability may be determined with certainty. Bichât was aware that venous blood could not preserve muscular excitability as well as arterial blood, while Ludwig and Schmidt (57) subsequently showed that the artificial circulation in warm-blooded muscles of blood that had been freed from oxygen had no more effect than if there had been no such circulation; the excitability in fact disappears more quickly in some cases when a muscle is injected with venous blood than when it is quite blood-

less—which is no doubt attributable to the directly inimical action of CO_2 . Experiments to the same effect have been made with similar results on the excised frog's heart. When the air is much attenuated (under the air-pump) the spontaneous pulsations cease after about an hour, and the muscle loses its excitability to artificial (mechanical or electrical) stimuli. If the air is restored the pulsations begin again. Cyon, Klug, and Saltet (58) showed the dependence of cardiac movements upon the presence of oxygen in the frog's heart. It was filled alternately with serum containing O, and serum saturated with CO_2 ; regular pulsations occurred only with the oxygenated serum. Want of oxygen therefore asphyxiates the heart as in ciliated cells of unicellular organisms. This is principally due to paralysis of the cardiac muscles from lack of oxygen, as witnessed in the gradual disappearance of the spontaneous contractions of the heart, together with a corresponding decrease in excitability to artificial stimuli.

It is highly probable that other nutritive matters carried by the blood play a similar part to oxygen, while equally the elimination of other D-products besides CO_2 is essential to the preservation of excitability; little, however, has yet been done in the way of experiment. Martius ascertained for cardiac muscle that serum-albumen had a marked effect in restoring depressed action. When 0.6 % NaCl solution is circulated through a heart that is beating spontaneously, or from artificial excitation, the pulsations, at first vigorous, disappear almost entirely; then, after the heart has been brought to a stand-still, and shows no trace of movement even with the strongest excitation, not merely excitability, but even automatic activity, will return if blood and serum, or even alkaline salt solution containing serum-albumen, are run through the heart. Peptone and all other albuminous bodies (syntonin, or albumen, casein, myosin) fail to produce this effect. The exhausted muscle treated with these remains absolutely unresponsive with even the strongest excitation, whereas in every case, after circulation of blood or serum, it recovered its beats, or spontaneous pulsations. These experiments have not yet been tried on striated skeletal muscle.

V.—EFFECT OF TEMPERATURE ON MUSCULAR CONTRACTION

The vital manifestations of all protoplasmic tissues are much affected by the temperature of the moment. There is a lower limit of temperature for every organism, at which life is permanently, or at least temporarily, extinguished, as well as an upper limit at which, principally on account of the coagulation of certain albumens, such a fundamental disintegration of the structure occurs that restoration of the normal functions seems to be impossible. The absolute value of temperature varies enormously in different kinds of protoplasm, and even apart from the "immune" bacteria, many cases are known in which the movements of protoplasmic structures have been observed at a temperature far above 40° C. Within the maximum and minimum range of "obvious contractility," we may assume as a general rule that energy of the movement increases with increase of temperature. This holds for amoeboid as well as for flagellated and ciliated movements, and the various kinds of muscle form no exception. But while in the simpler forms of mobile protoplasm it is only possible to determine the upper and lower limits, as well as the "optimum" of temperature at which spontaneous movements of apparently unlimited duration reach their utmost rapidity, in muscle we are able to go a step farther in the analysis of phenomena.

We have already alluded repeatedly to the great influence exerted upon the manifestations of fatigue and death, by temperature; an effect denoted by increase of D-products with higher, and a corresponding decrease of these at lower, temperature. Along with these are certain changes in the time-relations, and form and magnitude (height) of contraction, which Gad and Heymans in particular have recently been investigating, and which may be viewed as a specific effect of temperature (60). If a striated, skeletal, curarised frog's muscle is properly cooled, and excited from time to time by an induction shock, it is found in the first place that the (isotonic) curves of contraction are more extended in proportion as the temperature is lower. Comparison of the accompanying curves (Fig. 45) shows that the period of rising energy in particular is much elongated, and the steepness of the ascending portion decreases regularly in ratio with the

approximate constancy of steepness in the descending portion. Yet this constancy relates only to a given upper portion of the curve. The final return to equilibrium occurs more and more slowly with decrease of temperature (and contraction residue).

There is a marked difference in the effect of cold, and of fatigue, with regard to the time-relations of muscular contraction: on cooling, the descending portion of the curve is as steep as, or steeper than, the ascending portion; but in fatigue, which equally prolongs the contraction-process, it is found by all authors to be less steep.

A second conspicuous effect, overlooked in earlier researches, is the rise in height of the contractions, visible within a certain range, on cooling. The lift shows an absolute minimum near the freezing-point (of muscle-substance), where no further alteration

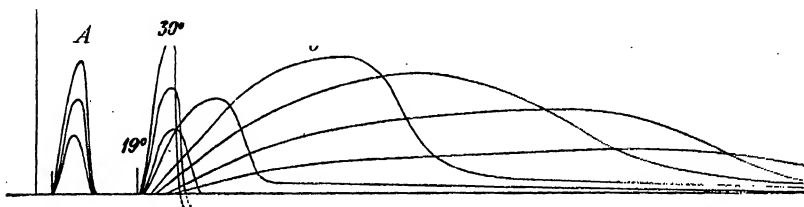


FIG. 45.—Schematic representation of isotonic curves of contraction at different temperatures. (–5 to +42½° C.) (J. Gad.)

in height can be observed on stimulation, and a relative minimum at about 19° C., from which point it rises to the absolute maximum at about 30° C., and the relative maximum at 0° C. The minimum duration of contraction coincides with the absolute maximum of lift, and increases constantly from this point, with falling temperature, until the contraction disappears. The latent period behaves like the period of contraction, increasing constantly with falling temperature. We have said that an absolute maximum of twitch was reached at about 30° C.; if the temperature rises beyond this, excitability and height of lift decrease more and more, while the duration of contraction remains approximately equal (Fig. 45, A).

At a moderate rate of heating it is possible to show that the excitability of muscle to electrical stimuli disappears almost entirely before the appearance of contraction from heat rigor. With the isometric method temperature of course produces the

same effect on single twitches, as in isotonic experiments. The only difference is in the form of the apex of the contraction curve. All isotonic curves are dome-shaped at the summit, *i.e.* diminution of the ordinates begins directly the maximum has been reached. In isometric curves, on the contrary, a plateau is formed by the interval between temperature of the room and freezing-point, at the summit of contraction, *i.e.* the maximum of tension remains constant for a longer or shorter time after it has reached its climax.

These striking effects of temperature upon the height and course of contraction in striated skeletal muscle seem to indicate that two different processes come into play during muscular activity, which are opposed to one another, and are differently affected by fall of temperature. Fick pointed out that a specific (chemical) process lies at the root of muscular relaxation, essentially differing from and opposite to that underlying contraction. The ordinates of the contraction curve are therefore not proportional to the intensity of *one* process, but express the results of two antagonistic processes. Fick suggests that the first of these may consist in the formation of a specific substance (decomposition of sugar into lactic acid), the second in the further disintegration of the resulting product (breaking up of lactic acid into H_2O and CO_2). The acid produces a partial coagulation of the contents of the sarcolemma, which is reduced again by removal of the chemical causes. Gad and several of his pupils, as also Schenk, have recently worked out this idea and applied it to the explanation of the phenomena under consideration (33). Here we need only say that the same conclusions follow naturally from Hering's general principle, and that it would be possible to explain all the phenomena observed on the supposition that change of temperature exerts a more depressive influence upon one of the fundamental processes of metabolism than upon the other.

On the hypothesis that the active "process of relaxation" in Fick's sense goes hand in hand with the process of assimilation, some value may attach to the observations of Fr. Schenk (61), *i.e.* that relaxation occurs more slowly in proportion with the scarcity of reserve substances in the muscle. On comparing an actively fatigued muscle with one whose excitability has been depressed by irrigating it with a solution of lactic acid, without

diminution of its store of reserve matters, it will be found that the latter relaxes more rapidly than the former. *The one behaves to the other as a cooled muscle to a fatigued muscle.*

There are no satisfactory observations as to the effect of temperature on magnitude and process of contraction in striated warm-blooded muscle, but it has long been ascertained for cardiac muscle both in cold and in warm-blooded animals, that the time-relations of the natural and spontaneous, as also of artificial, contractions, are considerably retarded by cooling, while the contrary occurs with rise of temperature. The mechanical latent period undergoes similar changes, most conspicuously in the excised heart of warm-blooded animals (A. D. Waller, 55). While at normal temperature (38° – 40°) the contraction apparently begins at the moment of excitation, a latent period being only perceptible on applying more delicate methods of time-measurement, on vigorous cooling (12° – 0°) it may last for more than a second. It is not known whether with uniform stimulation the same relations between temperature and contraction-magnitude obtain in cardiac muscle, as have been demonstrated by Gad and Heymans for striated skeletal muscle. If the normal period of contraction in a muscle is very short, the effect of falling temperature will be well marked, and on the other hand the shortening of the contraction process by warming is conspicuous when the muscle has previously been yielding a sluggish twitch. This is most marked in smooth muscle, where the process of contraction is accelerated in a remarkable degree by heating.

The behaviour of smooth muscle-elements with varying temperature exhibits many interesting peculiarities, mainly because in many, perhaps all cases, they fall into a state of more or less marked and permanent contraction ("*tonus*") independently of the nervous system, the strength of which is conditioned in a marked degree by the temperature of the moment. This is emphatically the case in the smooth muscles of many invertebrates, as well as in poikilothermic vertebrates. The adductor muscles of the fresh-water molluscs (Anodonta, Unio), *e.g.*, usually exhibit a well-developed tonus, which is certainly independent of the central nervous system. By partially breaking up the shell in large specimens of Anodonta, it is easy after removing the other soft parts to obtain a preparation which is well adapted to all kinds of excitation experiments (Fick, 32; Biedermann, 62). At

first the muscle is always so firmly contracted, that it not only resists the strong traction of the uninjured elastic ligament, but will even support a weight of more than 20 grs. without visible extension. Even when the shells gape sufficiently, after a long interval, to make effective excitation practicable, the efforts of the weighted muscle to shorten are still considerable, as shown by the fact that each decrease of its load is followed by a corresponding shortening. Even after many hours the presence of a certain "tonus" may generally be demonstrated. As soon as the insertion of the still living muscle is freed on one side, it contracts quickly to less than half its length with completely closed shell. In time, of course, this tonus diminishes slowly. If a preparation is left for several hours at medium temperature, the gradual relaxation can be easily determined. While at the beginning it takes considerable force to separate the two halves of the shell, this becomes gradually easier, and after several hours a weight of hardly 10 grs. will sometimes produce almost maximal extension of the muscle. When, therefore, the elastic ligament has not been injured in preparation, the shells, which were tightly closed at first, gape wider and wider, because the ratio between the tension in the opening ligament and the tonic effort of the muscle to contract, alters constantly in favour of the former.

The decrease of tonus, however, begins almost instantaneously if the preparation is submitted to a higher temperature (immersion in H_2O at about $30^\circ C.$), which soon effects a considerable relaxation. On subsequent cooling the tonus is only partially restored, though in other smooth muscles it comes back completely (63). Bernstein recently investigated the effect of different temperatures upon the muscles of the frog's stomach, arriving like Grünhagen and Samkow (64) at precisely the same results obtained by Biedermann from smooth molluscan muscle. Bernstein, after removing the mucosa, took a circular piece of the muscular layer, and stretched it between two hoops in a glass vessel, the shortening, or extension, being conveyed to a writing-lever by means of a thread running over a pulley. The medium of heating was either physiological salt solution, previously brought to the required temperature, and then poured into the vessel, or air saturated with steam. When treated in this way the ring of muscle corresponds exactly with the adductor muscle of molluscs

as described above. If any considerable tonus has been induced by the mechanical stimulation consequent on removal of the mucosa, it only yields very gradually at normal temperature. On the other hand, the lever drops with increasing rapidity if the temperature is raised about 25° – 40° C. If the muscle is tetanised during this period, the contractions obtained are much more vigorous, which is due less to increase of excitability than to diminution of tonus. Extension ceases between 45° and 50° C., simultaneously with excitability, and contraction first reappears at about 57° C., being then produced in great measure by rigor. Here we have the same fact as that demonstrated by Gad and Heymans in striated muscle, *i.e.* that excitability to electrical stimuli disappears almost entirely before contraction occurs from heat rigor. Previous to this, every cooling of the preparation had produced a contraction, *i.e.* a reinforcement or restoration of tonus. Grünhagen and Samkowcy confirmed the same reaction in the bladder muscles of the frog, while, on the other hand, many smooth muscles or warm-blooded animals (sphincter iridis, muscles of œsophagus) exhibit the contrary under similar conditions, contracting with warmth, and relaxing when cooled again. It must, however, be remembered that the effects of warming or cooling are essentially conditioned by the temporary state of the excitable substance, *i.e.* in the case above, by the degree of tonus. This again depends undoubtedly upon the conservation of normal vital conditions, in particular of normal temperature. It is therefore quite conceivable that the smooth muscles of warm-blooded animals may sometimes be atonic, when the corresponding elements of cold-blooded animals exhibited a marked tonus. This may account partially at any rate for the contradiction, in the above authors, as to the behaviour of smooth muscle in warm or cold-blooded animals. It is certain that *in living animals*, the smooth muscle of the blood-vessels relaxes locally when sufficiently warmed (application of a heated body to small exposed artery), and responds under these conditions like the elements of cold-blooded animals. Horvath (65) observed that the tracheæ of mammals widened on heating (relaxation of muscles), but became narrow on cooling (contraction of smooth elements).

Striated cardiac muscle also falls, under some conditions, into a state of permanent (tonic) contraction, and then presents a very favourable subject for the study of action of temperature upon

"tonus." External stimuli are for the most part the immediate cause of the latter, although a certain degree of tonus seems to be present under normal conditions without additional stimuli. We have frequently observed a persistent uniform state of contraction in the ventricle of the snail's heart (*Helix pomatia*), after a greater or lesser series of regular contractions consequent on sudden increase of pressure (Biedermann, 36). This condition is invariably developed in the same way in a heart attached to a canula and filled with snail's blood or 0.5 % salt solution. The ventricle at first extends itself *ad maximum* under the total pressure of the column of fluid in the canula, and empties again completely at each systolic contraction, but it is soon evident that the relaxation at diastole is incomplete. There is, so to speak, a contraction residue which grows with each successive contraction, until finally the heart ceases to relax, and remains in permanent (tonic) systolic contraction. The tonus may be resolved under certain conditions if the preparation is exposed to a higher temperature, while it reappears on cooling. This "cold tonus" apparently reduces much more rapidly on heating than the "pressure tonus." A single, momentary immersion in warm salt solution usually suffices to bring the contracted ventricle, with a scarcely perceptible "latent period," into the condition of complete diastolic relaxation.

A question which naturally belongs here, relates to the upper and lower limits of temperature at which a muscle is, generally speaking, capable of functioning, or at any rate can recover its capacity to function.

There is nothing surprising in the fact that muscle, like protoplasm in general, may be cooled to below 0° C., without permanent loss of excitability, for the freezing-point of the interstitial tissue-fluids, as well as that of contractile substance, must necessarily lie below zero. But it is difficult to say in detail what kind of changes the muscle-substance undergoes when its capacity of reaction is almost abolished by cooling. At all events the intensity of metabolism is reduced to a minimum. According to Gad and Heymans, restoration is impossible when reaction ceases entirely, upon which the excitable substance must have been injured intrinsically. This may occur either from its actual freezing, or from mechanical injury due to the freezing of the interstitial tissue-fluids. Kühne and Hermann, and more recently

Preyer, affirmed that hard-frozen muscles were still able to contract on thawing, and Waller finds the same for cardiac muscle. But in all these experiments it is questionable whether the contractile substance itself, or only the interstitial fluid, freezes.

VI.—EFFECT OF CHEMICAL SUBSTANCES UPON MUSCULAR CONTRACTION

The normal manifestations of muscular activity always betray more or less fundamental disturbance, when the chemical relations of the contractile elements undergo any material alteration. This appears already from the experiments we have been discussing, and in this connection the study of fatigue phenomena, which undoubtedly depend in part on the accumulation of certain disintegration products, is very instructive. Without entering into the action of all the many bodies whose effect on muscular excitability has so far been tested, we may quote some very cogent facts that are of importance to the sequel. In the first place, we must mention the curious and striking antagonism in the physiological action of the salts of sodium and potassium, which are in such close chemical affinity. Weak solutions of NaCl (0.5 – 0.6 %) have long been employed where a fluid is required to preserve the striated and smooth muscles, as well as the nerves, of vertebrates for as long as possible in approximately normal conditions. We are so accustomed on the strength of repeated experiences to regard “physiological salt solution”—the concentration of which must, of course, be adjusted to the content of salt in the tissue, and must therefore be correspondingly greater for sea-animals—as a perfectly neutral fluid, that it may well surprise us to learn from F. S. Locke’s recent observations (66) that this is only true to a limited extent, even in striated frog’s muscle. In experimenting with normal preparations of sartorius, and with preparations that had been lying for a long time in 0.6 % NaCl solution, he found considerable differences in excitability and curve of contraction. Single induction currents of great strength (“break” shocks in particular) sent through the entire muscle produced in salt muscles “tetanic contractions of enormous height and a duration of several seconds, after which the muscle relaxed suddenly, and showed only a slight contraction residue.” S. Ringer (67) had previously observed an inclination to

contracture in salted muscle, and found at the same time that it was entirely abolished by adding one part CaCl_2 to 5000 parts of the NaCl solution. Locke also observed that the high tetanic contractions described above disappeared after a short time, if the muscle giving this reaction was thrown into NaCl solution, plus a 10 % saturated solution of CaSO_4 . Here it would seem that a 0.6 % NaCl solution containing a calcium salt in the right proportion is more "physiological" than a pure unmixed solution.

NaCl solutions whose percentage is over or under 0.5 produce much more marked changes in the reactions of striated (frog's) muscle. In the first case, as Carslaw (68) found on circulating the fluid through the vessels of the posterior end of a frog, spontaneous excitation phenomena (tetanic contractions) appear very quickly, and last for several minutes, with intervening pauses. Solutions above 0.7 to 1 % NaCl produce, moreover, a shortening of the muscle, which resembles contracture, gradually increasing and diminishing again subsequently, while at 2 % the fibrillar twitches cease, and only a slowly increasing crenation, with corresponding loss of excitability, appears in the muscle. Previous to this point, single as well as tetanic shocks are accompanied by contracture. We may therefore say that within certain limits of concentration the excitability of striated voluntary muscle is considerably heightened or directly stimulated (chemically), by NaCl solutions, while at the same time a marked inclination to contracture is present.

This increase of excitability, and excitatory action of pure NaCl solution, are greatly increased by the addition of certain other salts of sodium, in particular of Na_2CO_3 . An uninjured frog's sartorius may be slightly excited when it is dipped into pure 0.6 % NaCl solution, as indicated by fibrillar twitches, but these are never of long duration. If, however, sodium phosphate (Na_2HPO_4) and a small quantity of Na_2CO_3 are added to the solution (5 grs. NaCl , 2 grs. Na_2HPO_4 , and 0.4–0.5 grs. Na_2CO_3 to a litre of distilled water) it will almost invariably be found that the immersed muscle, after a shorter or longer period of rest, sets up rhythmical activity, provided the temperature be not too high (3° – 10°C .) (69). In most cases this is first exhibited in a quick succession of weak, insignificant, and localised contractions, discharged at the same height from a greater or less number of primitive fibres. At times these movements are so

weak that they only appear in a very slight, but unmistakably rhythmical, tremor of the immersed muscle. Generally, however, these insignificant manifestations are followed at the same, or other, points of the fibre by stronger contractions, with a slower rhythm, which under some conditions cause the muscle to curve round in a semicircle towards the surface or border, or to roll up screw-fashion at regular intervals. For the rest there seems to be an inexhaustible variety in regard to the forms of movement, which may be observed in these reactions running parallel to, and interrupting, or not interfering with, each other, but all having in common that at the same point of the muscle, at a given time, there will be uniform rhythm of movement and incidence of stimulus.

It is by no means unusual, especially in the later stages of the action of alkaline salt solutions, to find that for a long time only one point of the immersed muscle continues in rhythmical activity, so that the preparation moves in the same constant rhythm as a beating heart, and this not infrequently gives rise to a phenomenon so strikingly like the "periodic function" of the frog's heart, described by Luciani (70), that the analogy of the two manifestations is at once apparent. These periods often occur suddenly and quite spontaneously after the preparation has pulsed for a long time in regular rhythm, the regular sequence of beats being interrupted by a longer or shorter interval. In other cases the appearance of the phenomenon is indicated by the fact that after a long series of pulsations of uniform rhythm, the pauses between every pair of beats become gradually longer, without in any way altering the quality of the single contractions. Finally there comes a long pause, and then a new series of pulsations, interrupted again by a period of rest, and so on.

At a low temperature the play of rhythmic activity may often be manifested for days. The phenomenon assumes a special interest when it is considered in connection with a series of recent observations by different experimenters upon the ventricle of the frog's heart, detached from the auricle.

Merunowicz, Roszbach, Stienon, Gaule, Gaskell, Löwit, and others have ascertained that the non-ganglionated "cardiac apex" of the frog may set up regular rhythmical activity when certain chemical substances which supply the nutrition of the preparation are added to a 0.6 % NaCl solution that is intrinsically ineffective.

This brings forward the question, which anatomical constituents of the cardiac apex are the first to be excited. Here, again, the muscles seem to be of primary importance, the more so since we have shown that curarised skeletal muscle is excited under almost similar conditions into analogous rhythmical activity. It seems to be an almost universal property of muscular substance to fall under certain conditions, with all prolonged stimuli, into a state of visible rhythmical excitation. Such a theory is not only supported by the foregoing facts, but by further observations on the rhythmical excitation of the sartorius and cardiac muscles with the constant current.

Apart from the "spontaneous" rhythmical phenomena of excitation, called out in striated muscle by dilute solutions of Na_2CO_3 , the specific action of this salt is also exhibited in a striking increase of response to artificial stimuli. This is very evident whenever a muscle that is not too thick, *e.g.* frog's sartorius, is treated wholly or partly with correspondingly dilute solutions. We shall presently refer to a very striking fact in this connection, which bears on the alteration in the effect of the constant current on a sartorius, half of which is treated with Na_2CO_3 . But even with localised mechanical stimulation, as well as with single induction shocks, or induced alternating currents, the increase of excitability asserts itself in a conspicuous increase in height of contraction, or tetanus curve, as well as by an augmented tendency to contracture.

The stronger solutions of Na_2SO_4 , as also very dilute solutions of NaOH (in 0.5 % NaCl solution), act like Na_2CO_3 , only in a less degree, so that seeing the identical action of these substances upon cardiac muscle, we are justified in speaking of a specific effect of the sodium salts in question, *i.e.* the contractile substance of striated muscle is so altered by the presence of even small quantities of these reagents, that it is excited more easily, and with smaller stimuli, than under normal conditions. The much-talked-of and frequently-tested action of *veratrin*—an alkaloid whose conspicuous effect upon striated muscle was first discovered by Kölliker, and subsequently investigated by Bezold (71), Fick, Böhm (72), and others—is to some extent comparable. While in the application of certain sodium salts, and of Na_2CO_3 in particular, it is the increase of excitability towards all stimuli that comes prominently forward, in *veratrin*-poisoning the extra-

ordinary prolongation of the contraction period (contracture) exclusively arrests attention. If a frog is poisoned with subcutaneous injections of 1–2 drops of, say, a 0.2 % solution of veratrin, after a short time a marked disturbance of the normal movements usually makes its appearance characterised above all by rapid and vigorous contractions, while the relaxation and elongation of the muscle, on the contrary, are very sluggish. This is still more plainly seen in experiments with isolated nerve-muscle preparations, especially when the changes of form are graphically recorded. While the ascending limb and summit of the curve betray no great alteration, the stage of falling energy is much protracted, and relaxation may be prolonged over many seconds. Since v. Bezold determined these remarkable effects of veratrin, it has been admitted that they are entirely due to an altered state of the muscle-substance proper, and depend, as Fick affirms, in all probability upon an “augmentation of the excitatory process beyond normal limits.” In order to produce maximal extension of contraction, it is advisable to give larger doses of the poison; we have found it convenient to introduce 6–7 drops of a 1 % solution of veratrin acet. into the posterior lymph sac, killing the frog (*R. tempor.*) after ten minutes at the latest. Seven minutes usually suffice to develop the symptoms characteristic of the poison. In the first place may be mentioned the more or less pronounced convulsions of the posterior extremities, which occur at short intervals, and are preceded by a general disturbance and spasmodic gaping. One unmistakable symptom is that the muscles of the belly go into protracted tetanus when mechanically excited, *e.g.* on pinching with forceps, as also occurs in a preparation of the sartorius when the nerve is divided. The rapid twitch at the moment of division is often succeeded, after a short pause, by a further, slowly increasing contraction, which remains constant for some time, and only gradually yields to relaxation.

If the changes of form in such a veratrinised sartorius are recorded, by fixing it between the stumps of bone left on either side to Hering's double myograph (which will be described below), one of the two movable non-polarisable electrodes having previously been fixed permanently, the same curves are usually obtained, whether the excitation is produced by an induction shock sent into any part of the muscle, or by minimal closure of a

battery current. In either case the waves of contraction are, as it were, fixed in their passage through the muscle, and a more or less prolonged, nearly uniform tetanus ensues, or, as it is better expressed in the absence of almost any evidence of discontinuity in the contraction, there is a "tonic" shortening in all the parts of the entire muscle.

As already shown by Bezold and Fick, different forms of contraction may be distinguished in the veratrin muscle, one of the commonest being that in which the peculiar tonic, persistent contraction is preceded by a more or less pronounced and rapid introductory twitch. As shown above, there is a rapid maximum contraction at the moment of excitation, followed immediately by a considerable extension, succeeded in its turn by a second slow contraction which only gradually yields to relaxation (Fig. 46).

Indications of this characteristic contraction are rarely absent, especially if the preparation is immersed for a

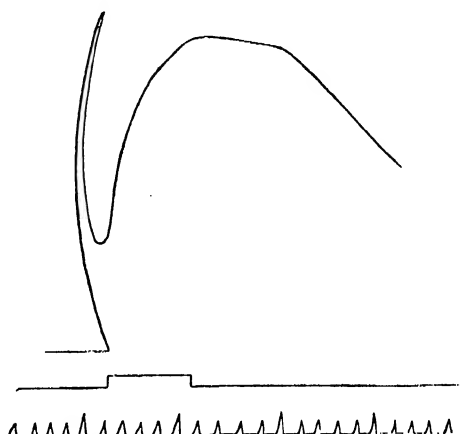


FIG. 46.—Make-twitch of veratrinized Frog's sartorius (1 Daniell). The characteristic tonic contraction is preceded by a rapid initial twitch. (Biedermann.)

long period in dilute salt solution. As Fick showed, the initial twitch cannot be explained by indirect excitation of the muscle from the intra-muscular nerves—the subsequent persistent contraction only being due to direct excitation of the muscle—for the same curves are exhibited after previous curarisation. The phenomenon may presumably be related to the fact first observed by Grützner, of the constitution of muscle out of two morphologically and functionally different kinds of fibres, corresponding to the red and pale (sluggish and quick) muscles. This view receives support from the fact that the same double-topped curves of contraction are not infrequent under other conditions, *eg.* local treatment with Na_2CO_3 , or even in perfectly normal frog's muscle. In sartorius itself Grützner finds it to be the rule. If the veratrin

muscle is repeatedly excited during the stage of relaxation by a short closure of the constant current, its response to the make excitation will generally be less in proportion to the height of its contraction during the previous stimulation. It not infrequently happens that the muscle, even when fully relaxed, will hardly give any perceptible response to the same stimulus that recently elicited a marked contraction. But in the majority of cases the increment of excitation effects proceeds *pari passu* with the progressive relaxation of the muscle, so that the twitches served up during the latter period at equal intervals, and of very brief duration, all rise to a uniform height above a line of abscissa—corresponding with the descending portion of the curve traced by the muscle after a single excitation. Fick made similar observations with indirect excitation (*via* nerve) of a veratrinised frog's muscle (72, p. 146).

As we have said, the character of the twitches alters in a marked way with rapidly repeated excitation, relaxation soon occurring as quickly as under normal conditions. If the muscle is left for some time unexcited, the first renewed contraction again exhibits all the characteristic veratrin effects. Temperature is an important factor, since the typical contraction-curve of the veratrin muscle is most pronounced at medium temperature, and less characteristic alike in great heat and in cold. In both these cases (Lauder-Brunton and Cash, 73) the phenomena of veratrin contracture disappear, to return again when the cooled or heated muscle is restored to a medium temperature. But the recovery is not invariable, so that it would appear as though the veratrin effect can be permanently abolished by change of temperature.

Barium salts act like veratrin upon the substance of striated muscle, while the *potassium* salts in general act as a muscle poison, depressing excitability more or less quickly, and finally abolishing it. This is to a marked degree the case, even with highly dilute solutions, so that, as indicated by Ranke, the salts of potassium presumably play an important part among the "fatigue products" of muscle. It is certain that both with localised applications of K salts, and on circulating them in solution through the muscle, every characteristic manifestation of muscular fatigue is produced, which can again be entirely cancelled by simply washing out the preparation with 0.6 % NaCl solution.

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VII.—SUMMATION OF STIMULI AND TETANUS

We have so far been considering single twitches only, as yielded when a muscle is excited by stimuli of short duration. It remains to be seen how a muscle reacts when two or several stimuli succeed each other at diminishing intervals. If the pauses are long enough to allow the muscle to relax completely before the commencement of each new contraction, a *series* of twitches is produced, in which each is completely separated from the others, and only affected indirectly (as in the staircase, or fatigue) in regard to magnitude and process of contraction. But if the intervals are lessened, and the stimuli (single induction shocks) succeed each other more rapidly, a limit will soon be reached at which the new stimulus begins to take effect before the first, or subsequent, twitches are completed, so that the muscle is hindered from ever returning to perfect relaxation. There will thus be a certain contraction remainder, which is in

ratio with the stimulation frequency, and at which the muscle in a measure oscillates. The more rapid the sequence of stimuli, the more tense will be the contraction of the muscle, and the smaller the individual rhythmical oscillations, which finally betray themselves only by a slight irregularity of the "tetanus curve" in a tracing, or to the eye by a slight tremor of the shiny surface.

Finally this "incomplete" fuses into "complete" tetanus, in which visible changes of form can no longer be detected. The muscle reaches its maximum of contraction soon after the commencement of the tetanising excitation, and the summit usually lies in this case much higher than in the (maximal) single contractions; during the persistence of the intermittent excitation it remains uniformly contracted, and returns rapidly to rest (as a rule) when this is over. In spite of its apparent steadiness, tetanus—as follows directly from its origin—must be regarded as a discontinuous process, arising out of a summation of single twitches, which are only prevented by the sluggishness of the muscle from expressing themselves in visible mass-movements, while—as we shall see—the internal, molecular changes do clearly and unmistakably reveal their intermittent character.

The manifold varieties of tetanus forms of contraction are only to be understood when the *laws of summation of stimuli* under the simplest conditions are familiar to us. Here again we are indebted to Helmholtz (1) for the first fundamental investigation. He led two maximal induction shocks into the nerve of a muscle in rapid succession, by opening two primary circuits behind the same secondary coil, one after the other. If the second excitation fell in the latent period of the first, it produced no effect, and the curve of contraction showed no difference from that traced by the first alone. But if it fell later, the relations of the corresponding curve would be the same as if the second stimulus had ensued during the resting stage of the muscle. "From the point at which the second excitation becomes effective, the twitch behaves as if the contracted state of the muscle at the moment was its natural state, and the second twitch alone induced in it" (Fig. 47).

Let (a, b, c) be the contraction curve of the first excitation, and (d, e, f) of the second, in their separate working, then the actual curve according to Helmholtz's law would correspond to

the line (a, g, h, i, k). We can readily see that the height of the summated twitches must be greatest, *i.e.* doubled, when the interval of both stimuli, like the stage of rising energy, is a simple contraction. This rule naturally loses its significance when several uniform stimuli follow successively at equal intervals, since a maximum of contraction is soon reached and cannot be exceeded. On the other hand, it is possible that each individual stimulus in incomplete tetanus may produce an equivalent period of rising energy. V. Kries, however, showed that this does not occur, even with summation of only two twitches. As is obvious from the above scheme, the apex of the summated curve must coincide with that of the second single twitch, or lie vertical to it, if Helmholtz's law is of general application. According to v. Kries (2), however, this is not the case. In 1886 he pointed out that in summated contractions the maxi-

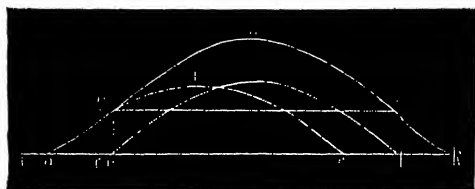


FIG. 47.—Schema of superposition of two twitches. (Helmholtz.)

imum of shortening was reached much sooner after the second excitation than in a single twitch, *i.e.*, in other words, the period of rising energy is shorter in the second twitch than in the first. If, with v. Kries, we denote the interval at which the apex of the summated twitches succeeds the second stimulus, the "apex-time," and the magnitude of the ordinates of the summated twitch the "apex-height," we find that (as above) in a series of "rising" or "falling" summated contractions (*i.e.* in the period of ascending or diminishing energy), discharged by two maximal induction currents, the "apex-time" decreases with a rising "apex-height" (Fig. 48). This is expressed in the accompanying series of curves, in which the place of the second stimulus remains unaltered, while that of the first can be moved to any distance; the apex of the summated twitch falls so much farther from the first stimulus in proportion as it lies higher. If we compare a rising and falling summated twitch, it will be found that the "apex-time" of the first is higher than that of the

second. The shortening of the apex-time is much more obvious in incomplete tetanus, when the period of rising energy often appears to be reduced to the third or fourth part of the time which it takes in single twitches.

Moreover, we learn from the relations of height in a contraction which is the sum of two simple twitches, that the theory, by which the later of the two is regarded as a single contraction upon a different abscissa, is not legitimate. Kronecker and Hall

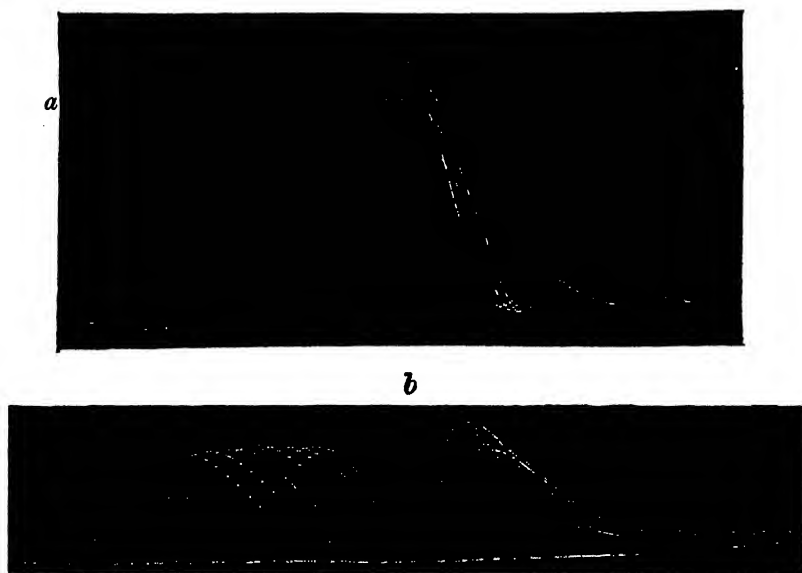


FIG. 48.—*a*, Series of ascending; *b*, series of descending summated twitches. The place of the second stimulus is the same in both cases, and only the first varies. The apex-height of the summated twitches inclines towards the left. (v. Kries.)

(3) found the height of "ascending" maximal contractions to be greater at first than would correspond with Helmholtz's law, but so much the smaller afterwards, according to the degree in which the second contraction superposed itself behind the earliest twitch. The greatest energy was developed by the second impulse when it fell in the first $\frac{1}{6}$ of the primary curve of contraction. The curve does not then proceed as if the state of contraction of the muscle at this moment were its point of rest, the second twitch only being excited, but the impulse of the first twitch is still effective. In the second and third $\frac{1}{6}$ the second

twitch helps the first, pretty much according to Helmholtz's law, while in the case where the second contraction rises from the summit of the first, the height of the summated contraction is always less than would correspond with the rule.

We have already considered the effect, where, on repeated excitation with equal, maximal, induction currents, the height of twitch grows in the form of a "staircase." The significance of this fact to the consequences of summation has been pointed out by Ch. Richet (4) in particular. He chiefly investigated the striated muscle of crab, in which the increase of excitability with repeated and uniform stimuli is very marked. Even in the case in which the single stimuli individually excite only sub-maximal twitches, and exhibit hardly any perceptible change of form (are "subliminal"), they may, on repeated application, become effective, because each single excitation increases the muscular response to the next stimulus (*addition latente*). Fig. 49 demonstrates very forcibly this effect of repeated uniform stimuli, each *per se* ineffective, upon the muscle.

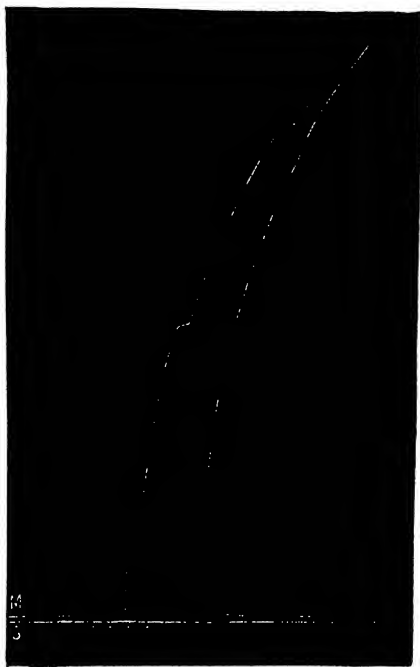


FIG. 49.—"Addition latente"; muscle of Crab; increasing effect of seven consecutive single stimuli (induction shocks), each ineffective *per se*. (Ch. Richet.)

The two first stimuli had no perceptible action, the third stimulus produces a minimal contraction, the fourth, one somewhat greater, while the three subsequent stimuli produce very marked contractions, which are fused into an incomplete tetanus. It is clear that such a dependence of excitability upon a previous excitation must sensibly affect the height of a summated twitch, as well as the magnitude of the tetanus shortening. And thus

it becomes intelligible that under certain conditions the height of a summated twitch may far surpass that of its two components.

It was shown above that the magnitude of interval between each pair of stimuli must not exceed a certain limit, if the beneficial effect of the preceding stimulus is to be observed upon its successor, and it is intelligible that under some conditions tetanus may be set up in the muscle, in consequence of a rapid succession of weak stimuli, although these in themselves would produce no visible change of form in the muscle. The intensity and frequency of stimulation necessary to produce such a *summation* (Richet's *addition latente*) must of course depend upon the nature of the muscle. As a general rule, sluggishly reacting muscle is more predisposed to summation of stimuli than quick muscle,

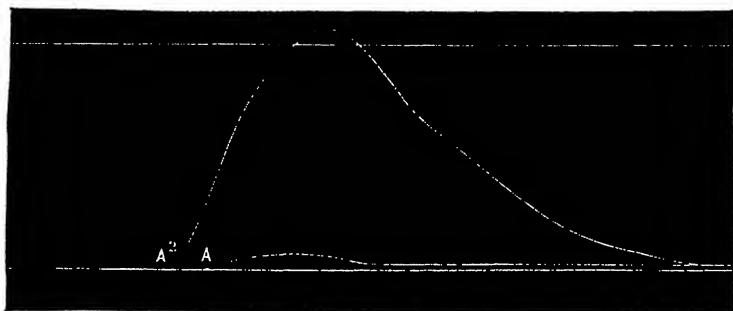


FIG. 50.—A, Simple twitch (muscle of Crab); A², summated twitch, from two closely approximated stimuli of the same magnitude as A. (Richet.)

which tallies with the rapid expiration of *all* phenomena of excitation in the latter, since the persistence of any kind of change in the muscle-substance resulting from a stimulus is the necessary condition of a subsequent heightening of excitability. The comparatively sluggish striated muscle of the heart may be indicated as peculiarly suited to summation effects in the above sense. Basch (5) showed that subliminal, single, electrical stimuli, inadequate in themselves to produce any contraction, will gradually (*addition latente*) increase the excitability of the heart-muscle (frog) if led into it at short intervals, until finally contractions will be discharged. Engelmann (6) made similar observations on the bulbus aortæ of the frog's heart, which also exhibits unmistakable effects of summation when rhythmically excited; the most obvious instances, however, are in *smooth* muscle. Here

it often happens that even with the most favourable conditions, the strongest *single* induction shocks scarcely produce any visible effect of excitation (contraction), while the same parts (intestine, ureter, muscle of mollusc) are thrown into tetanus by the rapid succession of stimuli from a vibrating Neff's hammer, at compara-

FIG. 51.

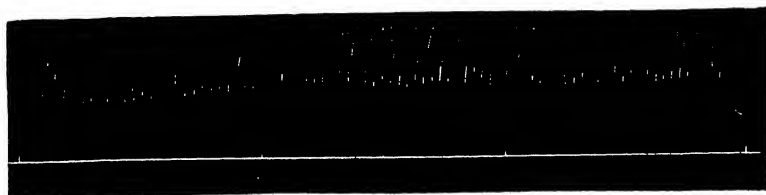


FIG. 52.



FIG. 53.



FIGS. 51-53.—Muscle of Frog, indirect excitation with induction currents of increasing strength at uniform frequency (10-12 per sec.) (Griitzner.)

tively high coil frequency. With the constant current, too, it may often be observed that with repeated closure at fairly short intervals, a current ineffective in itself will gradually produce effectual excitation (Engelmann). This property of summation of stimuli characterises all irritable protoplasm (ciliated cells, nerve cells, vegetable protoplasm, *e.g.* *Dionæa*, etc.) in a more or

less modified degree, so that the phenomena described in muscle are only a special case of a universal principle. Viewed in the light of the relations which we have been urging between an increase of excitability produced by excitation, and the process of excitation itself, it is a matter of indifference whether the process be regarded as a true "summation" of ineffective into effective stimuli, or as increase of excitability produced by this summation.

The following points with regard to form, process, and magnitude of tetanus contraction, and its dependence upon different variable factors, have been established by careful researches on the striated muscles of vertebrates and invertebrates. When the stimuli are weak, and the frequency per sec. moderate (10-12), the curve obtained from frog's muscles resembles Fig. 51.



FIG. 54.—Tetanus arising from, and resolving into, single twitches. The beginning and end of the tracing only are represented. In the omitted, central portion of 1.9 sec. the line traced by the muscle was horizontal. (Engelmann.)

This will be recognised as very incomplete tetanus, with deep indentations, so that only in a minor degree can the muscle be said to be permanently shortened. The summits of the indentations lie almost horizontal. If the exciting induction currents are strengthened, or increased in frequency, the teeth become shorter and flatter, and the indentations less deep; the muscle reaches a much higher degree of permanent contraction (Fig. 52). Finally, the curve rises steeply from the beginning, and the indentation becomes negligible, disappearing altogether in complete tetanus (Figs. 53, 54). According to Kohnstamm (9) the tetanus becomes more incomplete with uniform frequency, in proportion with increasing strength of stimulus, since every increment of stimulation accelerates the relaxation of the single contraction (Fig. 54).

Bohr (7) finds that the tetanus curve of unfatigued muscle (frog, toad) is "an equilateral hyperbola brought to an asymp-

tote," which is the more remarkable since the increment of single twitches in the "staircase," as well as with increasing strength of stimuli, follows the same law; yet the rule can hardly be universal, *e.g.* the tetanus curve of hydrophilus muscle does not coincide with it (Rollett, 8). The difference of contraction magnitude is at once apparent on comparing the two cases of complete tetanus resulting from a series of maximal induction shocks, and a single contraction. The freely contracting, loaded muscle invariably shortens more in tetanus than in a single twitch. Even if it were certain that the greater height of tetanus may be explained by the superposition (as described) of single twitches, the subsequent course of the process remains in obscurity. We can only conclude from the fact that the muscle in tetanus does not exceed a certain maximal shortening, that Helmholtz's law loses more and more of its significance with progressive superposition, each new stimulus being so much the less effective in proportion as the muscle has already shortened with the preceding stimuli. The height of the tetanus curve grows with the strength of excitation, or, where this is constant, with its frequency. The steepness of the rise alters in the same proportions (Kohnstamm, 9).

A fact of great importance in the estimation of tetanus was determined by v. Kries and v. Frey (10), who showed that artificial support of the muscle would, under some conditions, produce the same degree of contraction from a single stimulus, as in complete tetanus. In this experiment an adjusting screw is placed under the muscle-lever, and so arranged as to raise it to any given height. The loading first takes effect fully upon the muscle, when it begins to raise the lever from the support. The fact that the supported muscle contracts as vigorously in a single twitch, as the unsupported muscle in the more pronounced tetanus, is very apparent when single twitches and tetani are alternated in the same experiment. If the muscle is sufficiently loaded, the tetanus curve rises more or less above the summits of the single twitches of the unsupported muscle. If the tetanus is followed by a row of "propped" twitches (Fig. 55, *a*) the parallelism of the two processes is very apparent, and the conviction is forced upon us that in summation of twitches in muscle there must be some kind of under-propping in the muscle; the effect is, as Grützner (11) says, "as though the muscle contracted

so effectually in tetanus, because in some measure it forms its own support, and carries itself" (Fig 55).

In detail, we find many variations with regard to alteration

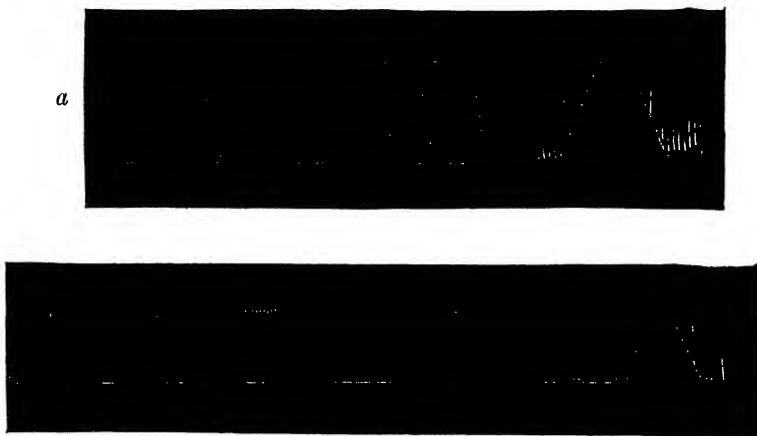


FIG. 55.—*a*, Gastrocnemius (Frog); single twitches, tetanus, and group of supported twitches, loaded at 10.5 gr.; *b*, the same at 0.5 gr. loading. (v. Frey.)

of height in a series of supported twitches. The highest summit of the curve either coincides with the highest adjustment of the supporting screw (as in the above example), or it may be reached

earlier, in which case the height of the twitches sinks again with further increased propping. Finally, there is the case in which height of twitch at first increases with regular progressive support, then decreases and finally rises again to the highest increment, so that the function has two maxima (v. Frey, 10–12) (Fig. 56).

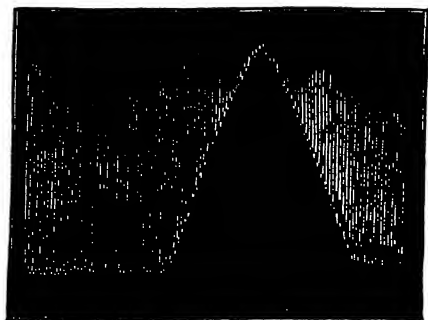


FIG. 56.—Curarised muscle; series of twitches with varying support; load, 6 grs.; stimulation interval, 1 sec. (v. Frey.)

These relations also are expressed in certain forms

of tetanus curves with two and three summits.

All these facts relate to the proportionately loaded muscle. With very light loading, on the other hand, the supporting

has little effect upon the position of the summit of the twitch, and in correspondence with this the difference between height of tetanus and height of twitch vanishes (Fig. 55, *b*). This is intelligible when it is remembered that at low tension the external conditions of the process of contraction cannot be intrinsically altered by the support. Tetani *lower* than the single twitch are frequent in fatigued muscle (Fig. 57). When a muscle has had a short rest after a prolonged series of contractions, the first twitch on the renewal of excitation is abnormally high in proportion with the following (Buckmaster's "initial" twitch), and this reversal of relation continues even if the muscle is supported.

At present there are insuperable difficulties in the way of any adequate explanation of all these relations, and, in particular, of

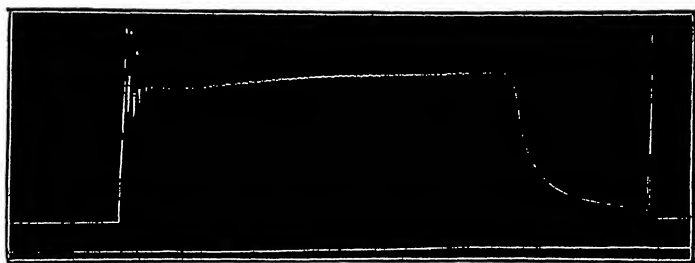


FIG. 57.—Tetanus and single twitch of a fatigued and curarised muscle; load, 10 grs.; rate of stimuli, 0.1 sec. (v. Frey.)

exact analysis of the process of tetanus, as is readily understood when we consider the number of different factors in the tetanus curve. The *staircase* appearance, *superposition* in Helmholtz's sense, the effect of internal *supporting*, as well as *fatigue* and *contracture*, all take more or less share in the process of tetanus (v. Frey).

Another and probably important factor is, that in the majority of cases a muscle is not a physiological unit, but represents a mixture of at least two functionally different elements, which can hardly be supposed to act simultaneously and uniformly. This leads to the further question of the dependence of tetanic excitation upon the nature of the muscle. Here, in the first place, we must consider the widely varying duration of contraction in different muscles, or the different fibres of the same muscle. An uninterrupted tetanus, where the twitches are superposed as above, can of course be expected only when the interval of stimulation is

equal to, or smaller than, the duration of twitch up to the moment of maximal shortening. It follows immediately from this, that to yield a complete tetanus the single stimuli must succeed each other the more rapidly in proportion with the shortness of the twitches. In the case of a twitch as rapid as that of the wing-muscles of certain insects, which lasts hardly $\frac{1}{300}$ sec., more than 300 stimuli per sec. would be required to produce a tetanus. When in other cases the contraction, as in the muscles of the tortoise, lasts about 1 sec., two stimuli per sec. will produce complete tetanus. This is most striking in the smooth muscles, which are so sluggish that it is conceivable that an incomplete tetanus may be produced, even when the single stimuli (repeated closure of a constant current of adequate strength) are separated by pauses of several seconds.

The following numbers give an approximate idea of the stimulation frequency per sec. required to produce tetanic fusion of twitches :—

Tortoise	2 (Marey)
Frog, Hyoglossus (slow)	10 to 15
„ Gastrocnem. (quick)	30
Crab, Claw-muscle (slow)	20 (Richet)
„ Tail-muscle (quick)	40
New-born animal (warm-blooded)	16 (Soltmann)
Rabbit (red muscle)	4 to 10 (Kronecker and Stirling)
„ (pale)	20 to 30
Bird	100 (Richet)
Insects	300 to 400 (Marey, Landois)

It is obvious that the above figures would vary considerably if the state of the muscles were to alter. We have already emphasised the difference in duration of twitch according as the muscle at the time of experiment is fresh or fatigued, with circulating blood or bloodless, is normal or poisoned (veratrin), warmed or cooled, so that without changing the frequency of stimulation we may have, according to the physiological state of the muscle, complete or incomplete tetanus, or only simple twitches. Moreover, a glance at the table given above shows what a significant difference exists in the stimulation - frequency required to tetanise functionally different striated muscles in the same animal. As these relations are of great importance, they must be examined more in detail. Ranvier (13) first drew

attention to the remarkable physiological differences between red and pale muscles in the rabbit, and more particularly to the enormous differences which he found in the stimulation-frequency required to produce tetanus, while Kronecker and Stirling (14) subsequently ascertained that the red muscle of rabbit, in correspondence with the sluggish process of contraction, is thrown by 4 stimuli per sec. into incomplete, by 10 per sec. into fairly complete, tetanus. With stimulation intervals of $\frac{1}{3}$ sec. the pale muscle recovers its extension again almost completely, while the red, though trembling, remains tensely contracted. The pale muscle of rabbit requires from 20 to 30 stimuli for complete tetanus. Analogous curves are obtained from corre-

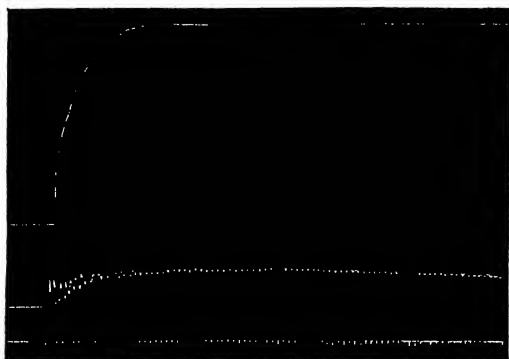


FIG. 58.—Tetanus curve of tail- and claw-muscles of Crab with uniform excitation. The quick tail-muscles fall into incomplete clonic tetanus, the sluggish claw-muscles into complete tetanus. (Richet.)

sponding excitation of the quick tail- and sluggish claw-muscles of the crab (Richet, 4) (Fig. 58).

Very characteristic, and functionally weighty, differences of tetanus contraction were found by Rollett (8) in the anatomically and physiologically different muscles of *hydrophilus* and *dytiscus*. Besides the fact that in this case also the quick, rapidly-contracting muscles of *dytiscus* require a higher stimulation-frequency to enable them to contract than the sluggish muscles of *hydrophilus*, as at once appears from Fig. 59, *a*, *b*, another important difference exists in the course of a prolonged and complete tetanus. The first tetani yielded by freshly-prepared *dytiscus* muscles rose more steeply, and fell much more rapidly, than those of *hydrophilus* muscles, in which the long duration of

the tetanus is highly significant. This is expressed in the fact that the height of the tetanus alters little with repeated excitation in hydrophilus, while in dytiscus it rapidly decreases. "Hydrophilus muscle, notwithstanding its excitation, remains capable of functioning for so long that it only becomes exhausted very gradually, provided it is given a short rest between the pro-

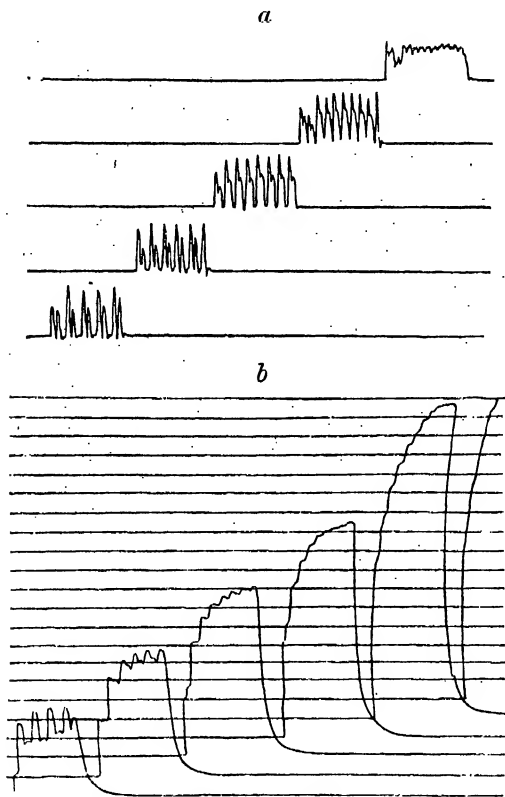


FIG. 59.—Tetani, *a*, of *Dytiscus*; *b*, of *Hydrophilus* muscle at uniform excitation. (Rollett.)

longed periods of activity in regular order of succession. *Dytiscus* muscle, on the contrary, is exhausted by exertion in a comparatively short time, but if it is given longer rest between the periods of exhaustive activity, it can, in spite of repeated efforts, recover itself between times to a certain extent in the intervals." Dissimilation and assimilation must accordingly take a different course in the two kinds of muscle. Richet (*l.c.* p. 114) made

similar observations in regard to the process of tetanus with prolonged excitation, in the sluggish claw- and quick tail-muscle of the crab. Complete tetanus of the latter is never of long duration, the muscle quickly relaxes, and for some time exhibits a marked diminution of excitability; the tetanus of the claw-muscles, on the other hand, increases gradually, and may persist for a long time. The relation of this phenomenon to the normal activity of both kinds of muscle is unmistakable. The powerfully developed adductor of the claw has to remain uniformly contracted for a long period with a great output of energy, while the tail serves up quick movements (strokes) like a rudder, and is concerned less with a prolonged yield of energy than with rapidity of motion.

These results are an additional confirmation of the conclusions which we have shown to stand out *re* energy and duration, from the distribution and presence of sarcoplasmic and non-sarcoplasmic (light and dark, *i.e.* pale and red) muscles. The same facts assume a still greater importance when it is remembered that in the majority of cases *one* muscle contains *both kinds* of functionally different fibres in varying quantitative relations. And if this double composition appears sometimes in a single, simple twitch, and is plainly expressed in the curve, the same also occurs, and in a much more marked degree, in tetanus. Generally speaking, we may expect that muscles, the bulk of which consists chiefly of sluggish (dark, red) fibres, will exhibit properties in conformity with these, while, if composed of quick fibres, they will react like the latter.

This is well indicated, according to Grützner (15), in the relation between the height of the single twitches and the height of tetanus. In loaded muscle the latter considerably out-tops the former; but under uniform conditions the difference is much more marked in sluggish than in quick fibres. If, *e.g.*, with direct excitation, the height of tetanus in the mixed gastrocnemius in frog and toad are compared, it will be seen that the muscle of the latter, which mainly consists of sluggish fibres, will raise the same weight much higher than the corresponding muscle of the frog, although it is much smaller. The former almost curls itself into a ball with strong electrical stimulation, while the frog's muscle, even in the most pronounced tetanus, is far from being rolled up. While in the "quick" muscles of the frog

(triceps, gastrocnemius) the height of twitch to that of tetanus is as 1 : 2-3, the ratio in the same muscle of the toad is about 1 : 5, and it is considerably larger in the more sluggish muscles (hyoglossus and rectus of frog, 1 : 8-9). In investigating isometric muscular action in man (*M. obductor indicis* or *interosseus dorsalis primus*) by a specially constructed tension indicator, Fick (16) found, on comparing the tension produced by a maximal single stimulus with that developed by tetanising excitation, that the latter is ten times as great as the former, while in the frog the difference is much less, whether in isotonic or isometric action. Human skeletal muscle therefore reacts in complete correspondence with red sluggish fibres.

Bearing in mind these results, which show that the work yielded in tetanus by the quick (pale, clear) muscles is insignificant both as regards size of weight lifted and height to which the load is raised, in comparison with the same yield of the sluggish (dark, red) muscles, we may adopt Grützner's denotation of the latter as "tetanus muscles," since they may be said, through their physiological properties, to be adapted to this form of shortening, and singularly fecund in their response. When quick and sluggish fibres are united in the same muscle, it may result from the differences of excitability as above, that with weak excitation (direct, or from the nerve) different portions of the muscle twitch, or go into tetanus, from those brought into play with stronger excitation. Grützner is even inclined to ascribe the summation-effect in tetanus in great part to these differences in the physiological response of the two kinds of fibres. He refers (11, p. 250) the striking similarity between a series of "supported" twitches, and tetanus (*supra*), to an internal supporting of the muscle by its sluggish (dark, red) fibres. These keep it at rest at a given medium length, which naturally decreases inversely to the number of red fibres. If an appropriate stimulus, *i.e.* not too powerful, is sent into the muscle when thus shortened, its excitable (light) portions will contract visibly. This second superposed contraction must accordingly result more quickly, as v. Kries found actually was the case (shortening of apex-time). The stronger the stimulus, however, the greater will be the activity of the more sluggish portions; the more rapidly will the discontinuity vanish (which, as might be expected, is disputed by Kohnstamm), and the greater will be the height of the "tetanus curve."

"This then affords a simple explanation of the fact, which is easy to confirm, that twitches may be elicited from a muscle that is already in steady and uniform contraction, as follows indeed in a great number of cases" (Grützner).

Upon this assumption, which, as it seems to us, emphasises one of the most essential and important factors that comes into play in tetanus contractions, "a tetanus remains discontinuous and unstable as long as the twitches of the pale fibres can be superposed upon the contraction of the red. But if the red have shortened to their maximum, the entire muscle will be so short that the twitching movements of the pale muscles produce little or no discontinuity of movement, or tremor."

On account both of its histological and physiological properties, cardiac muscle naturally falls under the same category as the sluggish, sarcoplasmic, striated skeletal muscles. In correspondence with its sluggish twitch and prolonged duration, we might naturally expect to find it peculiarly adapted to steady, complete tetanus. Yet the contrary results from experiment, and in this respect, as in many others, cardiac muscle takes up a characteristic attitude. Summation experiments are the more readily carried out on the heart, since its spontaneous rhythmical contractions, which are undoubtedly valid in a physiological sense as single twitches, may be employed in a slow series of beats (frog's heart) to investigate the action of a new artificial stimulus (induction shock) in different phases of contraction and relaxation. In these experiments Marey (17) found that cardiac muscle in certain phases of its activity was variably sensitive to excitation by a single induction shock, while during one period it is not at all excitable (refractory). The ventricle, and all other sections of the heart, are unresponsive to moderate stimuli during the entire systole of the parts in question, while in the diastolic period, as well as in the pause between each stimulus, an extra contraction is yielded. With stronger excitation this "refractory period" is more and more abbreviated, and very strong stimuli seem finally to produce an excitatory effect in every sphere of cardiac activity (Marey, Tigerstedt, Lovén, etc.). This remarkable property of all cardiac muscle will partially explain the characteristic reaction of the heart during a rapid succession of (tetanising) stimuli; for it is evident that in consequence of this peculiarity a constant, or rapidly repeated, excitation must fail to produce any

continuous, or summated, contraction (tetanus); there can only be a series of contractions interrupted by marked pauses. Bowditch was the first to determine by excitation of the frog's heart that even where the single induction shocks are separated by intervals of several seconds, the number of the contractions is often less than that of the stimuli. This disproportion between stimulus and contraction is even more striking where the former are working in quick succession, when the muscle of the heart will often fail to respond to a whole series of excitations (Basch, 5). Under these conditions a new cardiac rhythm, dependent on in-

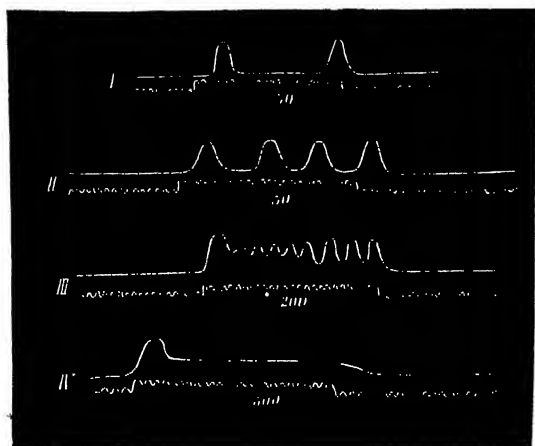


FIG. 60.—Bulbus aortae (Frog), tetanising excitation with induction currents. Stimulation-frequency, 80 per sec. Tuning-fork tracing, $\frac{1}{4}$ sec. The ciphers under the figures give intensities of tetanising currents. Intensity of coil pushed home=1000. (Engelmann.)

tensity and frequency of the stimulus, is always developed, since, as Engelmann (6) found on tetanising the bulb of the frog's heart with alternating currents, a very low excitation-strength will, after some time, produce a systole by "latent summation," followed perhaps by another, or several. The latent period of the first, and the intervals of the subsequent, contractions, are longer in proportion as the single stimuli are weaker. With growing density of the exciting current the duration of the latent period soon becomes minimal, as also the interval between each systole (Fig. 60). Even with the strongest currents Engelmann found no complete relaxation of the bulb after the first contraction; it remained in tetanus at a certain height.

Yet we have here no true superposition of contractions, but the first lift is of the same height as after a single effective stimulus. At first, interruptions may still be seen in the tetanus curve, the period of which is not, however, that of the stimulus, but longer, intrinsic to itself, and determined by the specific nature of the muscle-substance. Ranvier (18) obtained the same tetanus curves from the ventricle of the frog's heart. It cannot be doubted that this reaction of the cardiac bulbar muscles to tetanising excitation stands in the closest relation with their highly-developed faculty of *rhythmical* activity; we know that perfectly constant stimuli, *e.g.* chemical and mechanical, produce rhythmical contractions of cardiac, and also under certain conditions of striated skeletal, muscle during the entire duration of their action; this property is, however, much less developed in the latter than in the former.

We must assume that a series of single stimuli would approximate the more closely in their physiological effect to the action of a persistent stimulus, in proportion with the rapidity of succession of the stimuli, so that it would not be surprising if, under certain conditions, the effect of a *succession of stimuli* corresponded with that of a *persistent stimulus* in striated skeletal, as in cardiac, muscle. This does, indeed, appear to be the case, and two phenomena especially are remarkable as claiming attention in this particular, *i.e.*, on the one hand, the *rhythmically interrupted tetanus*, on the other, the so-called *initial contraction*. Richet (4, p. 126) was the first to describe rhythmical alterations in the curve of tetanised crab's claw-muscle, for which it appears that weak and very frequent stimuli are essential. Schoenlein (19) (Fig. 61, *a*, *b*) soon after made similar observations on beetle muscles (*dytiscus* and *hydrophilus*). He obtained, on exciting the muscles in the detached femur with induction currents of low strength and high frequency, either rhythmical contractions (*dytiscus*), or rhythmically interrupted tetani of longer duration (*hydrophilus*, crab), or finally contractions, separated by pauses of rest at different intervals. The stimulation-frequency in these experiments was usually 880 per sec., but the phenomena may be observed at much higher frequencies. The lower threshold is in the beetle 100 or 80, in crab as low as 30 per sec.

As regards current strength, the rhythm varied between

minimal stimulation distance and 1-2 mm., a very small interval of difference. With closer approximation the rhythm always passed into a smooth, unbroken tetanus. Here, again, the difference already pointed out between the muscles of *hydrophilus* and *dytiscus* is apparent, since, as we have seen, the former, like the sluggish claw-muscles of the crab, yield longer, rhythmically interrupted tetani, while the frequent rhythmical contractions characteristic of *dytiscus* under the same conditions are nowhere present. We have no hesitation in claiming for these

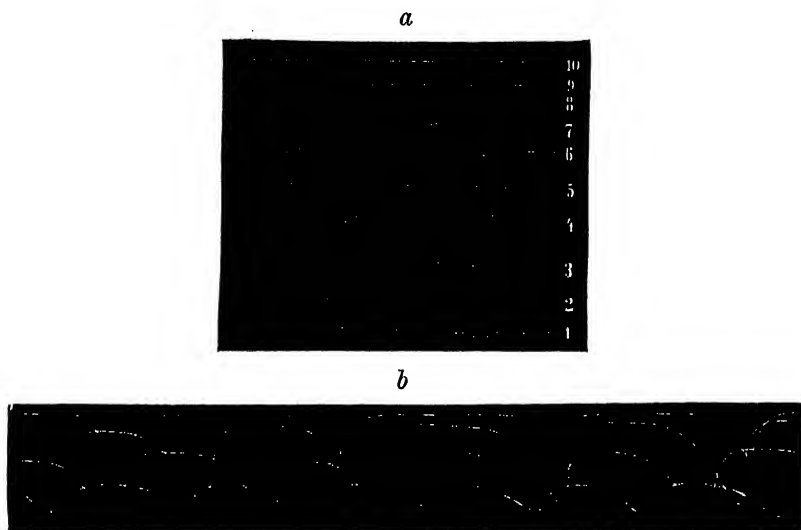


FIG. 61.—a, Rhythmical contractions of leg of *Dytiscus marginalis* with tetanising excitation. Stimulation-frequency, 880 per sec. b, Rhythmically interrupted tetani from leg of *Hydrophilus piceus*. (Schoenlein.)

observations of Schoenlein and Richet an analogy with the fact that cardiac muscle also yields rhythmical contractions under the same conditions, although, of course, we have in these to reckon besides with the value of the single twitches, which is never or rarely the case in beetle muscle. In the quick muscles of *dytiscus*, in which the frequency of rhythmical contraction varies at an average of 2-6 per sec., exceptionally rising to 30, it is perhaps legitimate to credit the single contractions with the value of single twitches, while the sluggish *hydrophilus* and crab muscle throughout exhibit short tetani. We shall presently see that cardiac muscle always, and striated skeletal muscle under at

least some circumstances, are stimulated by the constant current to quite analogous rhythmical activity. As a rule, however, the constant current only produces a single contraction when it is closed, and eventually when it is opened also (make and break twitch), in striated muscle, both with direct or indirect (*via* nerve) excitation. Interrupted currents have exactly the same effect under certain conditions.

Bernstein (20) was the first to observe that with a given frequency (about 900 per sec.), and moderate intensity, induction currents led into the frog's sciatic produced a single brief "twitch" of the gastrocnemius, a so-called "initial twitch," instead of tetanus; this is more apparent in the most rapid interruptions of the primary circuit, grows weaker with diminishing frequency of stimulation, and disappears entirely below a certain limit (200 to 300 stimuli per sec.) The phenomenon occurs with both direct and indirect excitation of curarised muscle. According to Grünhagen (21) and Engelmann (22) there is occasionally a "final twitch" at the close of the tetanus also, corresponding with the opening twitch of the constant current. The investigation of the effects of very high stimulation-frequencies on muscle (and nerve) often leads to contradictory results, because the application of electrical stimuli of great rapidity presents great technical difficulties, where complete uniformity in strength and order of succession is required. Neither the application of sliding contacts, nor mercury closure, is in this respect sufficiently trustworthy. Even Kronecker's "acoustic current interrupter" (14), in which the longitudinal vibrations of a magnetised iron rod, produced by friction, set up induction currents in a wire coil, fails, according to Roth (23), at very high frequencies (over 4000 vibrations). Roth (*loc.*) has recently employed the *microphone*, and obtained reliable electrical stimuli of high frequency, which were also regular and perfectly under control. Pipes of different pitch were blown by means of a gas motor, and a dry cell, equal to one Leclanché, was introduced into the primary circuit. With indirect excitation of a frog's gastrocnemius (from the nerve) Roth found that tetanus disappeared when 5000 stimuli per sec. were sent in from a pipe of 2500 vibrations, with a given strength of the Blake microphone. The limit with *direct* excitation of the muscle lay under similar conditions about 300 stimuli lower. V. Kries suc-

ceeded in obtaining oscillations of great frequency by the use of induction coils, produced by the rotation of a disc between the free surface of the iron axis of a coil, and the opposite pole of a powerful electro-magnet, the periphery of the disc consisting alternately of iron and a non-magnetic substance (brass). Since each iron tooth of the disc is magnetised as it passes over, a corresponding change occurs in the magnetism of the iron axis of the coil, and current is induced. The frequency of current-oscillation is equal to the number of iron teeth which run between the iron core and the pole of the magnet in a unit of time. (A similar apparatus was constructed later by Gritzner.)

Roth, as well as v. Kries, showed that an upper limit of the stimulation-frequency at which tetanus can still be called out exists only relatively. "For each intensity of current given as the amplitude of an oscillatory process, a frequency may be determined which need only be exceeded in order to produce disappearance of excitation effects." In order, therefore, to maintain a tetanus, intensity as well as frequency must be augmented, otherwise the phenomenon of the initial twitch will ensue, which is described by Roth as a very brief tetanus, while Schoenlein (25) regards it as a *single* twitch due to the summation of ineffective stimuli. V. Kries (*l.c.*) also finds that the time-relations of the initial twitch correspond throughout with simple induced twitches. If the frequency in a given case remains constant, and current intensity only diminishes, the effect remains approximately constant (Kraft, 26). An appearance analogous to the "initial" and "final" twitches was observed by Engelmann (6), during very frequent rhythmical excitation, in the smooth muscle of the rabbit's ureter, where "the close of a series of periodically recurring, short stimuli acts like the break of a constant current, just as the impact of a rapid succession of shocks acts like the closure of a constant current." We have made similar observations on the adductor muscle of *Anodonta* (27). And an effect corresponding with the initial twitch may be observed in cardiac muscle: "If a succession of stimuli (induction shocks) which would produce a twitch after each pause of two or more seconds with unfailing regularity, are sent into the excised ventricle at intervals of less than a second, the first stimulus will be followed by a systole, the later at most effect a weak local action" (Engelmann, 22).

Returning to the consideration of steady, complete tetanus, we have next to ask whether the excited state of the muscle is really continuous, as it appears from the curve to be, or if, notwithstanding appearances, discontinuous alterations of condition can be demonstrated, which follow in the usual course, but are not expressed in corresponding form-changes. It is conceivable that the contractile elements of the muscle may be thrown into new equilibrium, and maintained at the same as long as excitation continues, by the stimuli which follow at a given rapidity; or we may assume not only the excitation, but also muscular contraction itself, to be a discontinuous process, in which a vibratory movement of the smallest particles of the muscle-fibres corresponds with each impact of stimulation. Experimentally, there is strong reason for supposing that electrical tetanus is really discontinuous, notwithstanding its apparent continuity. If we touch a muscle, or, better, a whole limb, that is in rigid tetanus, a vibration is easily felt which can be expressed objectively by delicate graphic methods, as well as subjectively in the so-called muscle-sound or muscle-tone, and by the tremor of the shiny surface of the muscle in tetanus, as Brücke (28) observed through the skin of a man's arm when suitably illuminated. Helmholtz obtained an objective demonstration of the vibrations of tetanised muscle by fixing a watch-spring or paper flag on to an elastic board, attached to the muscle (29). The springs vibrate consonantly when their own vibration period coincides with that of the tetanised muscle. And a thread attached to the tendon of such a muscle, and stretched tensely, falls, as Engelmann (22) showed, into longitudinal vibrations, which can communicate perceptible impacts to a light recording lever. Since, further, rapid vibrations (*e.g.* of tuning-forks) may be conveyed through air-capsules with perfect accuracy, the quick tremor of the tetanised muscle is able, without any noticeable change in its length, to set the lever vibrating at comparatively large amplitudes according to the above method, cf. Marey's *prince myographique* (Kronecker and Hall, 3; v. Limbeck, 30).

These facts are even more interesting in reference to the much-disputed question whether the natural, voluntary or reflex, persistent contraction of striated muscle is produced by a rhythmically self-repeating impulse, as in artificial tetanus.

Wollaston (1810) and Ermann (1812) attempted to apply

the *muscle-sound* in determining the discontinuous nature of voluntary muscular contraction (Martins, 31), and Helmholtz subsequently investigated the phenomenon more exactly. Like Ermann he started from the fact that when the masticatory muscles are forcibly contracted at night, with the ears closed, "a dull, humming sound is heard, the ground-tone of which is not intrinsically altered by increased tension, while the humming that goes with it becomes stronger and louder. Helmholtz then found that on tetanising his own masseter directly, and the brachial muscles of an assistant from the median nerve, by means of an induction coil standing in the next room, the muscle gave the tone of the *interrupting spring* instead of the normal muscle-bruit. This is a direct proof that vibrations do occur within the muscle, however constant its change of form may appear to be, and that a vibration actually corresponds with each single stimulus, for if the number of stimuli is altered, the height of the muscle-tone alters also, since within certain limits it always corresponds with the stimulation-frequency. That no alteration of form is to be seen in the tetanised muscle only implies that vibrations occur in the smallest particles, while the external shape does not alter, much as a rod that is vibrating longitudinally emits a sound, although no external change of form is visible. Moreover, as pointed out by Hermann, the muscle-sound could still be explained if the periodic process in tetanised muscle were not merely mechanical, since the rhythmical currents of action to be discussed below appear to be sufficient to account for them.

The experiments of Helmholtz indicate a high degree of mobility in the least particles of striated muscle, for he even detected a clear muscle-tone of corresponding pitch in electrical tetanisation of 240 stimuli per sec. Bernstein (33) subsequently endeavoured to determine the range in which it was possible still to detect a clear muscle-tone, *i.e.* to what limit the muscle-elements responded to the rapidity of the stimuli acting on them in electrical tetanus. By means of the acoustic current-interrupter (in which a vibrating spring of different tensions opens and closes the primary circuit) he stimulated the gastrocnemius muscles of the rabbit, partly directly, partly from the nerve, and convinced himself that the muscle-bruit can reach a very considerable height, since a tone of 748 vibrations still sounds loudly,

and one of 933 vibrations is faintly audible. At a frequency of 1056 stimuli, however, only a tone a fifth or an octave lower was perceptible. Lovén (34) places the limit of reaction in rabbit muscle much lower. When all due precautions were taken, he heard from *M. tibialis anticus*, on exciting its nerve with very weak induction currents at a frequency of 330–380 per sec., a tone which was nearly always a distinct octave below the tone of the interrupter; it disappeared on intensifying the strength of current, and reappeared finally at a certain intensity in *unison* with the exciting tone. In individual cases the two octaves appeared with medium stimulation, sometimes simultaneously, sometimes alternating with one another. But a true muscle-tone was never emitted at a higher frequency than 880 per sec., corresponding to a'' , which the muscle responded by a' , the lower octave. With higher frequency of stimulation a dull, muscular bruit only is heard, and no tone corresponding to it. Experiments in which the sciatic nerve was tetanised by the telephone gave similar results. With progressive alterations of pitch by singing into it the scale from g (198 vibrations) to g' (396 vibrations), Lovén clearly heard the whole scale given out by the muscle up to c' (264 vibrations); the d' was very indistinct, e' , f , fis' , and g , on the other hand, again produced clear, muscular tones, but they belonged to the lower octave. Kronecker and Stirling (14) had found that on stimulating the pale gastrocnemius of rabbit with a König's tuning-fork (180 vibrations), introduced into the induction apparatus, or with the rapidly-vibrating Wagner's hammer, the tone corresponding to the number of vibrations in the interrupter was heard with every characteristic of its pitch, "as if the conducting wires were sound conductors." But this experiment is not confirmed by Lovén. In every case, even on singing into the telephone, "the muscle-tone was conspicuously dull and low-pitched," only the ground-tone of its deeper octave being given out, never the over-tones. Wedenski's observations (35), which refer specially to the detection of the action currents of tetanised muscle by the telephone (*infra*), also indicate that the capacity of striated muscle to respond to very frequent stimuli by corresponding, rhythmical alterations of state, is limited. Previous to the upper limit of rhythmical stimulation-frequency, at which the muscle only replies by a dull, unmusical sound, an exception occurs to the rule that holds at the beginning—*i.e.* that pitch corresponds with

stimulation-frequency, since the tone produced is an octave, a fifth, or even two octaves lower. According to Wedenski there is complete parallelism between the electrical oscillations and the mechanical (audible) vibrations of the muscle, in the sense that the pitch of both tones is identical. The muscle responds to each very frequent excitation by a characteristic bruit, but not by a tone of corresponding pitch. The limit in warm-blooded muscles lies at about 1000 stimuli per sec.; in frog's muscle it is much lower; according to Wedenski this last ceases to give a tone corresponding with the stimulation-frequency at about 200 stimuli per sec. Lovén usually failed in hearing any mechanical tone (caused by vibrations) in the gastrocnemius of the frog, even with the help of the most sensitive instruments. This seems to indicate that the capacity of muscle to produce a musical tone in response to rhythmical excitation is the more developed in proportion with the mobility of the muscle, *i.e.* with the rate of its contraction. (Birds' muscles would presumably respond to very high frequencies; the pale muscle of mammals, according to Kronecker and Stirling, *l.c.*, far surpass the red in this particular; tortoise muscle emits hardly any sound, or only at a comparatively low frequency.) It also appears that the capacity of a muscle to give out sound suffers considerable variations if the mobility of the smallest particles is from any cause diminished. This specially applies to fatigue, to which is owing the fact that a muscle which, at the beginning of excitation, gives out a tone of corresponding pitch, subsequently produces a deeper sound, and eventually only an indefinite murmur (Wedenski, *l.c.*) Finally, the character of the muscle-tone depends also upon intensity of the single stimuli; where this is very low an undefined murmur replaces the musical tone at maximal excitation, in spite of an adequate stimulation-frequency.

The fact that the muscle-tone does not always correspond with the frequency of stimulation in direct excitation from the nerve, makes conclusions as to the rhythm of central innervation, deduced from the *natural* muscle-bruit, very uncertain. We have said above that muscles, when thrown voluntarily into vigorous and persistent contraction, emit a dull, humming sound. It is difficult to determine the pitch of the ground-tone in this case, because it lies on the threshold of perceptible tones. Helmholtz estimated it in his masticatory muscles at 36–40 vibrations

per sec. Wollaston had previously attempted to determine the vibration-frequency in voluntary contraction of his brachial muscles by supporting his arm on a grooved board, over which a rounded piece of wood passes with such rapidity that the sound is of the same pitch as the muscle-sound. He found that the frequency of the latter lay between 20 and 30 vibrations. Helmholtz subsequently found, by means of the consonating spring, that in voluntary innervation there was a marked and visible consonance, when the spring was registered, at 18-20 vibrations per sec.

It would appear from these experiments that the vibration-frequency of the natural muscular rhythm in man is not 30-40, but 18-20. What is heard as the muscle-tone is really only the first over-tone of the true muscle-vibration, the ground-tone of which is no longer within the range of audible perception: according to Helmholtz it corresponds with the C of the 16-foot open organ-pipe, and is like this a resonance-tone of the ear. We cannot therefore, from the pitch of the sound that is directly audible in voluntary contraction of the muscle, draw any direct conclusions as to the frequency of the central impulses. But the objective resonance experiments with consonating springs, as well as the observation of du Bois-Reymond, to the effect that a similar bruit is heard both in voluntary innervation and in artificial tetanus when the current is led into the spinal cord, and not directly to nerve or muscle, do notwithstanding appear to show that the natural rhythm of excitation from the central nervous system lies at about 18-20 per sec. According to du Bois-Reymond we hear, under these conditions, not the tone of the current oscillations, but a deeper tone, corresponding in every way with the muscle-bruit. Kronecker and Stanley Hall (3) obtained the same results from the objective registration of variations in bulk of the exposed M. biceps femoris of rabbit, by means of Marey's air-capsules. In agreement with the results of Helmholtz and du Bois-Reymond, the curve described by the muscle only showed 20 shallow undulations, when the number of stimuli led into the spinal cord was about 43 per sec. This seems to determine objectively that the central organ (spinal cord) not merely possesses an intrinsic rhythm of innervation peculiar to it under all circumstances, but that the number of efferent impulses also corresponds in general with the number of vibrations in the natural muscle-tone. Horsley and Schäfer found on tetanising the

cerebral cortex fillet, or spinal cord, that the rate of muscular vibration was much lower, the average of vibrations being only 10, when the stimulation-frequency was above 10 per sec.; the results of voluntary, persistent contraction also correspond with this lower value, and Canney and Tunstall (37) determined the same in man (cf. also Griffiths, 38).

V. Kries (39) arrived at similar results. He used apparatus constructed after one of Marey's sphygmographs: "A steel spring-plate is fixed at one end, the other free end carries on one surface a wooden peg about 2 cm. long, to which is fastened the little button—a thin disc of wood 1 cm. in diameter—that rests on the muscle. The other surface of the steel spring is provided with a sharp edge, which, as in Marey's sphygmograph, transfers the movements of the spring, greatly magnified, to a very light recording lever." When, after fixing the arm, the hand was bent sharply towards the wrist, v. Kries obtained curves from the flexor muscles of the under-arm like Fig. 62, *c*, with a distinct rhythmical periodicity of 11.8 per sec. The oscillations of the other muscles were still slower, *e.g.* the deltoid (weight held out with arm stretched horizontally) showed a rhythm of 9.6 per sec.; plantar flexion of the foot only 7.7. Hence it would appear that the number of impulses hitherto taken as the rhythm of central innervation, *i.e.* 18–20 per sec., is too high, and that with slow movements or persistent contraction it must, as a rule, be estimated at 10–12 per sec. But as v. Kries pointed out, both the rhythm of physiological innervation and the time-relations of the single impulse must vary within considerable limits, for the persistent contractions, due to voluntary innervation, are effected by 11–12 impulses per sec., while, on the other hand, we are also capable of making 11 single movements in a second (pianoforte playing), which rhythm must also necessarily be present in the innervation process. It may be concluded that in both cases—notwithstanding the coincident periods—the innervation must have varied considerably (v. Kries, *l.c.*)

As was remarked by Brücke (28), it is in the highest degree improbable that voluntary muscular movements are due to only one single efferent impulse from the cerebrum. In all cases, even the shortest voluntary "twitch" implies a short tetanus. This agrees with Barat's statement (14, p. 26) that "a voluntary contraction of the simplest possible character (tap with the finger)

generally lasts twice as long as the same movement excited by a single induction shock." V. Kries confirmed this, and was also able to show from the graphic record of the activity of the flexor muscles, with the quickest possible rhythmical movements of the middle finger or whole hand (9 per sec.), minute but quite visible oscillations, accessory to the larger waves, with an interval of $\frac{1}{36}$ sec. (Fig. 62, *b*).

If every experimental error from mechanical vibration is here really excluded, we must inevitably conclude with v. Kries that the rhythm of increase in the muscle, as in other cases, indicates the rhythm of the central impulses that impinge upon it. With a rapid sequence of short movements we should therefore have to picture the process of innervation as such "that our will presides over combinations of stimuli in which the single impulses follow with great rapidity, one predominating in each case over the rest

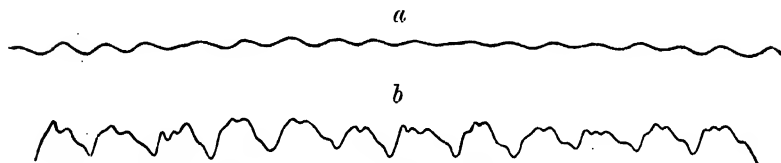


FIG. 62.—Oscillations with voluntary muscle activity. *a*, With strenuous, persistent contraction of muscles of the forearm (hand balled towards the fist); the spring rests on the volar side of the under-arm. *b*, Activity of flexor muscles on rapid rhythmic bending of the middle-finger. (v. Kries.)

to a marked extent." The extent and diversity of physiological reaction in quick and sluggish muscle, as above, are closely allied to the idea that along with slow and rapid movements there is also innervation of functionally different elements, the more so as partial innervation of one and the same muscle does undoubtedly occur. In favour of such a view, which needs much farther investigation, we may perhaps quote the observation of v. Kries that the highest frequency of motor impulses occurs, not with the development of the greatest power, but with the greatest mobility. "The most pronounced efforts were produced with low stimulation-frequency (10–12 per sec.)." If these last experiments militate against the theory that there is a constant invariable "intrinsic rhythm" of the central nervous system, this is no less the case in v. Limbeck's observations on the number of oscillations yielded by a muscle on artificial excitation of the brain or spinal cord by induction currents of alternating frequency (30). Both in warm-

blooded animals (dog, rabbit) and in those that are cold-blooded, the number of stimuli acting upon the central organ in a unit of time may be varied within wide limits without interrupting the

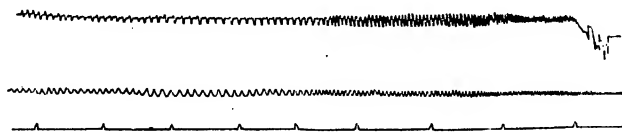


FIG. 63.—Tetanus curve of Rabbit with direct excitation of spinal cord. The stimulation-frequency varies between 10 and 34 per sec. (v. Limbeck.)

uniform rhythmical oscillations (longitudinal or lateral variations) of the excited muscle. This is very evident in the accompanying curve (Fig. 63)—obtained by direct stimulation of the spinal cord of rabbit—which shows most plainly how the number of muscular contractions per second increases with the number of stimuli sent into the central organ.

The stimulation-frequency varied in this case between 10 and 34, with prolonged tension of the spring of a Neff's hammer in the induction apparatus, the correspondence in number of the single contractions (oscillations) of the muscle being so exact that at the beginning even the make and break effects are visible in the curve, as shown by the greater and lesser indentations. The same results appeared from other experiments, in

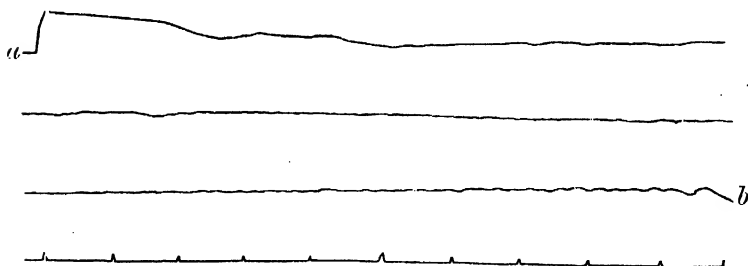


FIG. 64.—Muscular oscillations in strychnia tetanus (Frog). *a*, Commencement; *b*, end of the curve. (v. Limbeck.)

which a persistent reflex contraction of the muscle was obtained (central excitation of sciatic nerve of opposite side). V. Limbeck failed to discover oscillations in the myogram at stimulation-frequencies employed by Kronecker and Stanley Hall (43 per sec.), as well as Horsley and Schäfer; the curves were almost

unbroken. On the other hand, both in frog and rabbit very obvious oscillations (though of strikingly different rhythm) were produced by strychnia spasms. Fig. 64 shows that they vary in the frog from 2 to 3 per sec.; Fig. 65 from 10 to 19 in the

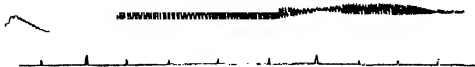


FIG. 65.—Strychnia tetanus of Rabbit. (v. Limbeck.)

rabbit. Towards the end of the spasm the oscillations became gradually less frequent, and are often grouped together (Fig. 65).

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VIII.—CONDUCTIVITY OF MUSCLE

A remarkable antithesis may in general be observed with regard to the property of transmitting localised excitation, between the relatively undifferentiated plasma of the Protozoa, characterised by flowing (amoeboid) movements, and the contractile *fibrils* differentiated from the same. In the former, localised and strictly limited excitation usually produces local effects only, in the most favourable instances distributed merely over the immediate vicinity, whereas in the differentiated, fibrillar parts, conduction is nearly always highly developed. In the majority of cases it has not been accurately determined whether the excitatory movements due to "cell-conductivity" in certain plants result from the transmission from cell to cell of the *exciting stimulus* (extension, traction) in consequence of alterations of turgor—comparable with its transmission in *Carchesium* colonies where the individual polyps are not in protoplasmic continuity—or of the actual *excitatory process* (alterations of the plasma).

In the latter case (*e.g.* excitable tissue of *Mimosa*) this would mean an extraordinary rapidity of conduction for undifferentiated

plasma, the more so since the mobility of the plasma in vegetable cells is on the whole but little developed, and stands at much the same level as that of the free-swimming *Amœba*.

It can, however, be demonstrated that conductivity increases *pari passu* with increased mobility and sensibility to external stimuli—a fact of which we have unmistakable evidence in Protozoa, on comparing the sluggish Rhizopods with the highly mobile Flagellates and Ciliata. In most Infusoria there is, on excitation, a specific conduction in minute motor organs (cilia, flagellæ), which must be regarded as a fibrillar differentiation; although in these cases the body-plasma itself seems to be the conductor through which excitation is transmitted with extraordinary rapidity.

The ciliary movements in localised excitation of Ciliata belong to this category. If, *e.g.*, *Paramecium aurelia* encounters any obstacle in swimming, the cilia of the body collectively make a stroke almost simultaneously in the direction opposed to the normal, thus jerking the animal backwards, after which the original movement begins again. A similar effect on the cilia, without simultaneous co-operation of the myoïdeum, may also sometimes be observed in this protozoan.

The contraction of the myoïdeum itself, the simplest muscle-element known to us, takes place as a rule so rapidly, that analysis of its time-relations in localised excitation is impossible. "If, *e.g.*, a *Spirostomum*, which owing to its extended form is the best adapted to this kind of experiment, is locally stimulated at one end only, contraction of the whole body will ensue, without any perceptible difference in time between the contraction of the anterior and posterior ends." "Hence it may be concluded that conductivity of excitation within the myoïdeum is excessively rapid; the effects of excitation follow immediately on the weakest stimuli without any perceptible latent period, while in the relatively undifferentiated rhizopod plasma there is almost invariably a pronounced time of latent excitation between stimulus and visible effects of stimulation" (Verworn). In both cases the myoïdeum reacts precisely like the most highly differentiated *striated* muscles, in which, however, notwithstanding the rapidity of transmission, the wave of contraction can be exactly measured. We are indebted to Aeby (1) for the first experiments in this direction; he used the graphic method to determine the course of the

contraction wave in two different points of the muscle (frog's gracilis). In the case of a muscle with parallel fibres, locally excited at one end only, the obvious consequences will be a contraction (expansion) of the part excited, which travels at great

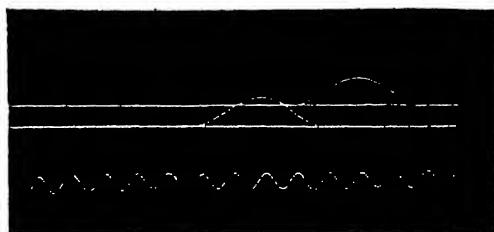


FIG. 66.—Velocity of contraction wave in muscle. The magnitude of interval between the two curves (of expansion) is the measure. (Marey.)

speed from the seat of excitation along the entire length of the muscle. Two given points in the continuity of the muscle will contract at different times, one after the other, and thus by means of two levers, each of which rises with the expansion of a given section of the muscle, the curve of expansion in both sections can be recorded upon a suitable myograph (Fig. 70). From the magnitude of the interval between the two curves standing upon the same abscissa, it is easy to calculate the rapidity at which the wave of contraction is transmitted (Fig. 66).

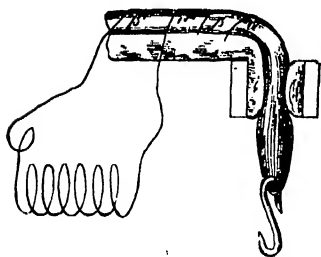


FIG. 67.—Rate of transmission of excitation in muscle. (v. Bezold's method.)

Similar results to those of Aebv were obtained by v. Bezold, 1861 (2), but with quite a different method. He fixed a muscle with parallel fibres lightly between two corks at its centre, so that direct transmission of changes in form was prevented, but not the propagation of the excitatory process; the lower part only (Fig. 67) recorded its contraction, and thus the time elapsing between an excitation at the upper end, and the beginning of the twitch at the lower, was determined; this would obviously correspond with the rapidity of transmission from the excited point to the first section beyond the clamp. The experiments of Aebv and v. Bezold gave the rapidity of transmission in striated frog's muscle

as about 1 m. per sec. (1.2–1.6 m.), but later investigations found a much higher velocity. Bernstein, *e.g.* (3), gives a velocity of 3.2–4.4 ms., on measuring the latent period of the curve of expansion in a given section of the muscle (gracilis and semimembranosus group in frog) when excitation was applied directly to the spot recording itself, and subsequently at as great a distance from it as possible. The experiment was arranged as in Fig. 68. It will be seen to consist in a modification of Aeby's

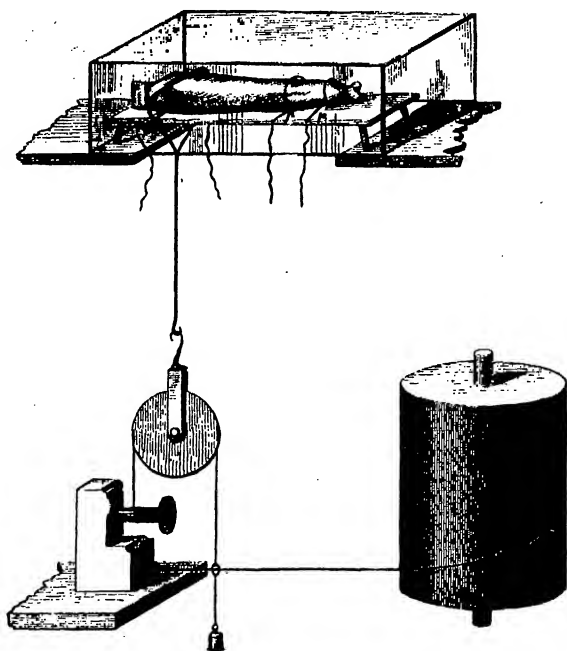


FIG. 68.—Rate of transmission of excitation in muscle. (Bernstein's method.)

method, in which, however, it is not so much the velocity of transmission of the *contraction wave*, as the underlying *excitation*, that is measured, its value being taken as identical with the former.

As the gracilis and semimembranosus muscles used by Aeby and Bernstein are characterised by a very oblique tendinous intersection, so that each muscle consists as it were of two completely separate portions, in which excitation remains isolated under all conditions, it seemed advisable to repeat the experiments with more suitable preparations. Hermann (4) accordingly employed the two sartorius muscles of a curarised frog

laid closely together, and determined the rapidity of transmission to be from 2 to 7 ms. From this experiment of Bernstein, the *duration and length* of an entire wave of contraction are easy to determine. If a muscle of sufficient length could be procured, we should be able, on exciting one end of the muscle, to follow the progress of the contraction wave with the unaided eye. This is prevented by the shortness of the muscle preparations practicable; but on the hypothesis that a muscle consists of physiologically homogeneous fibres, we have in the curve of expansion of any section an approximately correct picture of the process and duration of the wave of contraction, or more correctly of the alteration in condition of the muscular elements, while the wave of contraction is sweeping over them. The duration of the curve described therefore coincides with the vibration period of the wave of contraction. The rapidity of this wave being known, its *length* also may be calculated. When the wave w (Fig. 69) is at

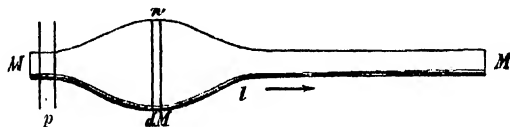


FIG. 69.

the point represented in the diagram, it has already passed the point of excitation p ; while at p , however, it has been transmitted as far as l . If its duration be termed (D), its length (L), and the rapidity of transmission (V), $L = VD$. According to Bernstein's experiments, the value of (L) is between 198 and 380 mm.

In contractile substances whose conductivity of excitation has been little developed, as, *e.g.*, in Rhizopoda (*Diffugia*), it is at once evident on exciting locally that the resulting changes are most pronounced in the immediate neighbourhood of the point of excitation, and become weaker in proportion as they spread by conduction (Verworn, 5). On touching a pseudopodium of *Diffugia* gently with the point of a needle, the manifestations of excitation (wrinkling, and extrusion of substance) are strictly localised. If the stimulus is strengthened, "the phenomena extend over the entire pseudopod, and are much more rapid and vigorous after repeated excitation so that the greater part of the pseudopod, and eventually

the whole of it, is retracted. The more distant pseudopodia, however, still remain unaffected, or retract only a very little, and that gradually." Finally, with very strong stimulation, the process of contraction may extend to all the pseudopodia, till the whole mass is withdrawn. "The stimulated pseudopod is drawn back most quickly, almost instantaneously, while the others follow more slowly in proportion with their distance."

It follows that stronger stimuli not only produce a quicker reaction than weak stimuli, but that the effects are more widely diffused, *i.e.* the effect diminishes with distance from the point of excitation.

Although it is *a priori* probable that the same is true of conduction of every excitatory process in all living substance, its direct proof is very difficult wherever excitability and conductivity are highly developed, since the difference, owing to the inconsiderable length of the tracts available, must be minimal. This notwithstanding, Bernstein succeeded in demonstrating that the wave of contraction in striated frog's muscle undergoes a perceptible diminution (a "decrement") during its course, whence it follows that the *expansion-curve* of a *directly* excited point of the muscle is invariably higher than that of a more distant point excited with the same stimulus. It must, however, be remembered that these experiments relate to *excised* muscles, in which nutrition is no longer normal, so that, as du Bois-Reymond pointed out, the decrement observed might well be a manifestation of the dying muscle. And, indeed, we shall see from certain galvanometric effects in uninjured muscle, to be discussed below, that a decrease in the excitation wave preceding the wave of contraction is not perceptible.

In view of the significant differences in velocity of the contraction process in striated muscles of different animals, and even in different muscles of the same species, it is not surprising that similar differences should exist in regard to *conductivity*,—the muscular twitch being in general only the expression of a contraction spreading itself from the point of excitation over the entire muscle. Accordingly the rapidity with which excitation, or contraction, is transmitted varies in the same instances and the same sense as the curve of the twitch, so that its rapidity may be said to vary directly with the magnitude of the latter. According to Hermann and Aeby the velocity in the tortoise averages 0.5–1.8 m. ;

and since this refers to the rapidly-moving M. retractor of the neck, the other muscles of the same animal must yield a still lower value. Bernstein and Steiner (6) found, as we should expect, that the rate of conductivity in warm-blooded muscles (sterno-mastoid of dog) was considerably greater than in cold-blooded animals (3–6 m.), and certain experiments of Hermann (*infra*) estimate it for living human muscle at between 10 and 13 m. per sec.

We are indebted to Rollett (7) for experiments on the rapidity of transmission of contraction in the red and pale muscles of rabbit, which notably present wide differences in regard to the

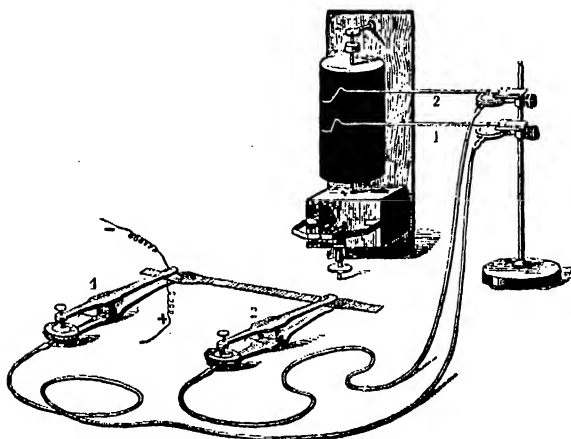


FIG. 70.—Determination of velocity of muscular excitation by the *pince myographique*. (Marey.)

time-relations of their twitches. After freeing the pale semi-membranosus and the red cruralis, he placed a strip 30–40 mm. long between the forceps of a Marey's *pince myographique* (Fig. 70). These were connected with a Marey's registering tympanum, by means of which the curves of expansion were recorded on a rotating cylinder, which also showed a tuning-fork tracing of 100 vibrations per sec. A make induction shock served as stimulus. The animals experimented on were curarised. The curve of expansion, corresponding with the excitation point, is again steeper and less extended than the transmitted wave, so that in estimating the time differences between the curves the interval at which they commence is the only datum. The physiological deviations of the pale (quick) and red (sluggish)

muscles are also exhibited here in regard to duration of expansion, which is greater at the excitation point of the cruralis than in semimembranosus. The rate of transmission per second in the latter is 5417–11,364 mm., in the former 3000–34,000 mm. The value of the red (sluggish) rabbit muscle therefore tallies with the rate of transmission (3500 mm. per sec.) determined by Bernstein and Steiner for the nictitating muscle of the dog. And if comparative observations on the velocity at which excitation is transmitted in the striated muscles of different animals thus establish a close ratio between the dying-out of the contraction-process at any point and the rapidity of its conduction, the same appears no less clearly from the fact that in a muscle preparation, where the length of twitch is altered experimentally in a *plus* or *minus* sense, the rate of conductivity is equally affected by the same data, *e.g.* in particular, fatigue (death), and alterations of temperature.

As in warm-blooded, striated muscles the length of twitch and general excitability diminish more rapidly after any injury than in those that are cold-blooded, so with conductivity—only in a much more pronounced degree; for it is always this property which is the first to suffer, and even to disappear, at a time when local excitability can still be easily demonstrated. The further investigation of these manifestations of decline in warm-blooded muscles presents many points of interest. Since the rate of conductivity diminishes constantly, and more rapidly than excitation, we seem to have at hand a simple means of following the wave of contraction with the unaided eye without artificial assistance. Schiff (8) was the first to demonstrate that local mechanical excitation, applied shortly after the death of the animal to an exposed muscle, produces a swelling which remains stationary, while two waves of contraction spread almost at the same moment on either side to both ends of the muscle. “While the contraction is proceeding, the parts adjacent to the now pronounced swelling relax. If the wave of contraction has reached the end of the muscle, it turns back towards its starting-point. But in the meantime a new wave has started from the point of excitation in both directions, which encounters the reflected wave and crosses it, and this interference repeats itself frequently, because each wave after crossing runs on undisturbed till eventually it grows weaker and dies out.” As the muscle becomes more and more moribund, and

loses its conductivity in proportion, the play of waves finally ceases altogether, although the persistent contraction still remains at the point of excitation, and was by Schiff regarded as the specific manifestation of muscular excitability, and opposed as the "neuro-muscular" twitch to the "idio-muscular" contraction. This local swelling appears most plainly on mechanically exciting (by a blow, or stroking with a blunt-pointed instrument) the moribund muscle of a dead animal, which no longer twitches with electrical stimulation. "The swelling appears slowly, and is delayed in proportion with the exhaustion of the muscle and length of time elapsed since the death of the animal." When the swelling has reached its maximum it maintains it for a longer or shorter time, perhaps several minutes, and then diminishes again comparatively slowly. In this way, especially when stroking at right angles to the direction of the fibres, it is possible to write and draw with a hard object on the upper surface of a suitable muscle.

Distinct idio-muscular swellings can seldom be provoked in fresh frog's muscle. The sartorius from a half-dried leg works better according to Hermann (9). "If such a muscle is stretched out on cork at a certain stage, every contact of a needle, especially with gentle cross-pressure, will produce a local swelling, which persists for some time. The same reaction is even better shown on cooled frog's muscle, in which both mechanical and electrical excitation produce a long-sustained contraction at the point stimulated. The contractile, palatine organs (containing striated muscle-fibres) of certain fishes (cyprinoids, tench) also exhibit well-marked, idio-muscular swellings.

These observations of Schiff, which may be compared with the older experiments of Bennet Dowler (Hermann's *Handb.* i. 1, p. 45, note) on the muscles of the human subject immediately after death, were subsequently confirmed, and extended in several directions, though the original interpretation of Schiff—to which Kühne also subscribed later—to the effect that the phenomena were merely the consequences of diminished excitability in the muscle, appeared somewhat dubious. The observations mainly refer to the appearance of the "idio-muscular" swelling, and the slowly-transmitted wave of contraction that proceeds from it in the muscles of the living human subject. After E. H. Weber, Ed. Weber, and Funke had exhibited upon themselves, by hitting the biceps or gastrocnemius with a blunt surface, idio-muscular

swellings which exactly resembled those on the muscles of the decapitated subject (a mode of demonstration to which Kühne subsequently referred as "familiar to every gymnast"), L. Auerbach followed up these effects more thoroughly, and communicated his observations in an essay, "Ueber topische Muskelreizung," published in the *Jahresberichten d. Schlesischen Gesellschaft*, 1861 (*Nat. Wiss., Med. Abtheilg.*, Heft 3). He produced local excitation by blows with a percussion hammer, and reported that very generally in man, and in many muscles of the body, an almost conical lump rises up on the spot thus percussed, lasting as a rule 3-5 secs. with comparatively no alteration, and then sinking slowly down again at the same point of the muscle. He refers some minor—apparently local—changes of the lump to the collective shortening of the muscle-bundle from the mechanical excitation. In many "rare" cases (Auerbach quotes four such individuals) there is, moreover, an undulatory manifestation, but he was only able to induce it in pectoralis major and the inner half of biceps by smart taps on a spot overlying the bone. This wave-like appearance consists of a low crest rising up on either side of the idio-muscular swelling, which gradually spreads like a wave on the surface of smooth water, at very moderate velocity, towards the two ends of the muscle. He never observed a backward motion of these waves in the human subject. On the other hand, it was very conspicuous in the rabbit, where he was able to provoke Schiff's play of waves on most muscles by gentle mechanical stimulation, *e.g.* tapping, or stroking vertically with a blunt object. According to A. Pick, the most favourable muscles are the ventral section of pectoralis major, and the sterno-mastoid. On stroking these muscles vigorously with the handle of a scalpel across the direction of the fibres, a linear swelling appears at the excited point, after a brief twitch of the muscle-bundle, while a flat, slowly-transmitted wave spreads towards the intersection of the muscle in one or both directions from the seat of excitation. After death this undulatory contraction always disappears before the idio-muscular swelling, which can still be provoked several hours later. Sometimes the swelling seems to bifurcate by the formation of a hollow at the point excited, while a wave spreads out on both sides towards either end of the muscle, and may eventually be reflected back again. The same has been observed in the living human subject by Baierlacher (12). Both these experi-

ments, and those of Erb (13) on highly-excitables convalescents after severe illnesses (*e.g.* phthisical subjects and others, in whom a tap on certain skeletal muscles produces a definite swelling, whence little waves of contraction extend to both ends of the muscle-fibres), go to prove that these manifestations are due not so much to depressed excitability of the muscle as to normal effects of excitation, which Auerbach regards as the direct expression of excessive excitability. Analogous observations of Chwostek (14) and Pick (*l.c.*) on patients (mostly lean, badly-nourished individuals) seem to indicate that the idio-muscular swelling may be regularly provoked in man, if not in all muscles or by every mechanical stimulus. Biceps brachii and the flexor group of the fore-arm seem particularly suited for the purpose. A firm support is, as may be supposed, conducive to the appearance of an effect of excitation, and the advantages of it are seen in exciting an appropriate muscle of any animal with uniform excitation before and after supporting it firmly. It is possible that the formation of the swelling in, *e.g.*, the lower limbs of very wasted subjects only, much more rarely on normal, healthy individuals,—may depend less upon a definite excitatory state of the muscle than upon the fact that such muscles are more favourable to the action of a mechanical stimulus. It is noticeable that under all conditions when the undulatory contraction appears along with the idio-muscular swelling, the muscle is still capable of twitching, so that *the same fibres could transmit rapid, as well as slow, waves of contraction*. The same is exhibited, as Kühne showed (*l.c.* p. 618), in perfectly fresh frog's muscle. Indeed, the manifestation is much more regular there than in the muscles of warm-blooded animals. If the sartorius is hung up by one end, and a cross-section made at the other with scissors, at the same time somewhat stretching the muscle, "so that the play of waves is not lost in retrograde twitches, the little waves will be seen in transmitted light, in which the muscle exhibits beautiful colours, apparently rising in the transparent mass, and subsiding again, so that there is a lively alternation of play of colour in the shimmering muscle."

Hermann (9, p. 604) made similar observations on the freshly-prepared sartorius, fixed to a cork-plate, and mechanically excited at any point by sticking in a needle, or pressing down a fine wooden chisel. From this point a minute wave or ripple usually

spreads over the fibres in both directions from the point excited, lasting as a rule a little longer than the excitation. Under these conditions there can be no question of referring the phenomenon to diminished muscular excitability. It appears indeed from Milrad's (15) experiments upon muscles of which the excitability had been raised or depressed by different chemical substances (veratrin, chloroform, Na_2CO_3 , caffèin) that the appearance of the idio-muscular swelling is favoured by diminution of excitability, and delayed by its augmentation, provided the difference between the normal and the poisoned, or fatigued, muscle is insignificant, and does not often exceed the error of observation, but that the slow undulatory contractions are only apparent with normal or increased excitability. Both Schiff and Auerbach state that the play of waves on stroking with a blunt needle appears only in the muscles of freshly-caught frogs, and Milrad says that this form of contraction may nearly always be produced if excitability is artificially heightened, or abolished if it is lowered. Since both the idio-muscular swelling and the wave-action may be observed in curarised animals, they are obviously the consequence of direct muscular excitation, although on many sides the theory has been put forward (chiefly on the ground of totally inadequate experiments, 16) that the motor nerve-endings take part in the muscle phenomenon under discussion.

Although mechanical stimuli are undoubtedly the most favourable to the production of the idio-muscular swelling, the application of other stimuli is by no means excluded. Auerbach, *e.g.* (*l.c.* p. 342), found that with local application of "weak" faradisation currents a lump was raised at either pole, while with stronger currents there was a marked swelling over the whole intrapolar area, as was afterwards confirmed by Milrad (*l.c.* p. 266). And further, we must regard the persistent closure contraction (*infra*) which appears at the kathode on sending in a constant current of sufficient strength in both striated and smooth muscle, as an idio-muscular swelling, while the wave of striated muscle (Hermann's galvanic wave), that may be seen to proceed from the anode under similar conditions, seems to be directly comparable with the wave-action on mechanical excitation.

As Rollett (7, p. 201 ff.) correctly pointed out, the muscles of insects must have an especial significance *re* interpretation of relations between the contraction wave and the manifestations

which appear in different forms of muscular contraction. Bowman first made observations on these muscles, and his results tally exactly with the preceding. Here we find an undulatory contraction in the *individual*, living or surviving, *muscle-fibres*, which may be directly observed with the microscope, and thus (as also from the excessive slowness of the process) exhibit minutiae that must always escape us in the entire muscle, where we have numerous fibres in very different physiological conditions. It is further possible to fix such short contractions during their course, by treatment with proper methods of hardening, so that the finest details of the changes which accompany the process of contraction in the muscle-fibres become visible. Even during life two processes of movement may be observed in the striated muscles of many insects, those which—corresponding with the twitch of vertebrate muscles—consist in the rapid, instantaneous contraction of the muscle-bundle *in toto*, and, on the other hand, knots or short waves spreading slowly over the fibres, which often arise periodically or rhythmically with no demonstrable external stimulus. Here again it is important to note that, as Wagener (17) pointed out with regard to the larva of *Corethra*, the fibres in which this wave-action is apparent were perfectly capable of producing total contractions (twitches). He repeatedly saw both forms of movement alternating in the same fibre, to which, however, it must be added that the wave-action does not appear in perfectly vigorous animals. Laulanić (18), who investigated *Corethra*-larvæ in every possible stage of dying, also makes a sharp distinction between the muscular movements of the vigorous animal and those of the surviving muscles of the dying animal. He regards the former (“secousses, contractions totales et simultanées”) as the expression of *normal* muscular activity; the latter (“ondes musculaires”) as the expression of intrinsic activity in the surviving muscles. Rollett (19) subsequently analysed both phenomena more exactly. He described the undulations of the muscles of dying *Corethra*-larvæ as follows: “The waves, at first few in number, in single fibres of the muscle visible only under the microscope, gradually appear in more and more of the fibres, and then repeat themselves in the same fibres at ever-shorter periods, so that a lively undulation ensues, which only dies away after a long time, as it came. The waves in the single fibres repeat themselves only at longer periods,

the number of fibres in which waves occur grows less and less, and after a time there are only a few, in which they spread at longer and longer intervals, until finally they appear in single fibres at very remote periods."

Since, as Rollett also affirms, the first, slowly-spreading waves appear in fibres that are still capable of total contractions (twitches), it cannot be doubted that the short waves also must be regarded as "peculiarly distributed processes of movement in normally active muscular substance, produced by specific excitation." These waves in the muscles of dying *Corethra*-larvæ, present the greatest similarity with the movements of freshly-excised insect muscles, as frequently observed since the researches of Bowman (20). Rollett studied these in long, narrow strips of muscle from a great number of beetles, in which the undulatory movement often lasted for hours. It usually reaches its maximum development at the first moment, where the particles of muscle are quickly examined under the microscope. Here, too, the waves appear as short knots rising and falling steeply, and spreading slowly in the fibres, and their length also is limited, including only from about 12 to 24 striæ. This limitation continues when the undulatory motion becomes less energetic, which happens again in this case, because the waves appear in fewer and fewer fibres at longer intervals, and finally only at prolonged periods in single fibres. If freshly-excised beetle muscle is covered quickly and examined under the microscope, a lively undulation is seen to be spreading over the fibre, but we are, as Rollett says, quite ignorant as to the cause of the undulations. They spread along the fibres, coming and going always in the same direction. Yet this is not invariably the case. Sometimes a definite starting-point of the advancing wave occurs in the middle of the individual fibre. This was demonstrated by Bowman, and later by Acby, on the transparent legs of certain small kinds of spiders. A swelling appears on the given point, which (cf. Acby) appears to rest for a moment on the crest of its progress, and then suddenly divides in such a way that the most swollen part sinks rapidly back to the original level, while the two halves separate and spread in opposite directions towards both ends of the fibre; where such a spot has once been found, it is easy to see that it forms for some time a permanent starting-point for new, periodic undulations.

According to Rollett, it appears as though the short waves, in many cases, arise in or near a section, from which inferences may be made as to the significance of the muscle-current, or the chemical changes concomitant with the death of the muscle-substance, as a discharging excitation. In individual cases the end-plate can undoubtedly constitute the point of departure for a wave of contraction, and this apparently applies to all the waves developed along one fibre.

Rollett tried to determine the rate of transmission of these waves in sufficiently long strips of muscle cut out of the extensors and flexors of the hind pair of legs, in large beetles, using the same method which E. H. Weber employed to measure the rapidity of the capillary circulation. The number of metronome beats was counted for the interval between the coincidence of the maximum with a given fraction of the scale, at the beginning, and at the end, of an ocular micrometer. Values were thus obtained of 0.08–0.67 mm. (average, 0.169 mm.); the length of the waves varied between 0.08 and 0.115 mm. Thus there are true “miniature waves,” which propagate themselves at such a low rate, that even the slowest waves of contraction in striated, vertebrate muscle, varying according to Auerbach from 314 to 371 mm. per sec., have a considerable velocity in comparison. Unfortunately it has till now been found impossible to measure the rate of conductivity of the excitation which provokes the *rapid* twitch in insect muscles. But it is certain that it must be considerable in twitches of short duration (0.0112–0.527 secs., Rollett), even on Rollett’s assumption, that the longest waves (transmitted at greatest velocity) of insects are far behind those of vertebrate muscle. Schiff and others, as we have seen, observed a *reflection* of the slow contraction wave in many striated, vertebrate muscles, when it reached the end of a fibre. A similar effect seems seldom, if ever, to appear in insects; Rollett at least has failed to discover, either in the entire muscle of *Corethra*-larvæ, or in excised beetle muscle, anything “that could be described as a reflected wave.”

Both in the case (*supra*) in which the wave arises in the centre of a fibre, and spreads to both sides, and in that where no definite point of departure is to be discovered, it may be seen to disappear suddenly, midway, with no previous diminution.

Interference between two waves of contraction coming from opposite sides (the two terminal sections of a fibre) was only *once* observed by Rollett, when the two waves at first united into one larger wave and then expired.

The "fixed" waves of contraction, described above, are due (as appears probable from Rollett, 19) to a kind of summation; they may frequently be observed in the muscle-fibres of insects killed in alcohol and osmic acid. They are usually distinguished from the waves of *living* muscle by their *greater length*, which Engelmann explains on the supposition that they were fixed while their rapidity of transmission was still considerable.

Rollett, however, assumes that "an entire series of short, consecutive, living waves were *partially fixed* in succession, so that they do not represent any single process, but are the sum of fixed parts of contraction waves in time order. If any given point of the muscle-fibre has for some time been the starting-point of short periodic waves, some of the contracted muscle sections will frequently, as Rollett says, remain fixed, while the adjacent muscle-sections on either side relax again. Thus a *persistent* contraction is produced in a short segment of the muscle only, and from this the remaining waves spread outwards. And it must be observed that each new wave that originates from the contracted section, itself gives rise to one similar section, while the rest relax again; in this way the area of fixed contraction grows longer and longer, till at last the whole movement is blocked, or ceases with a wave that dies out against the relaxed end of the fibre." Such fixed waves can rarely be demonstrated on the muscles of vertebrates, in which waves of contraction may of course be seen, but not the lively, persistent, spontaneous undulation (Bowman, *l.c.*; Nasse, 21). Doyer's expansion is very commonly the starting-point of undulation in insect muscle, and accordingly, the spot at which fixed waves of contraction are readily formed. Sometimes *partial* contraction is exhibited, the so-called lateral waves (*ondes laterales*) of fixed contraction. Rollett assigns this as a special characteristic of most Chrysomelid (7, p. 216) muscle-fibres, while in other insect muscles lateral waves of contraction occur rarely (*Tenebrionidæ*, *Curculionidæ*, and *Scarabæidæ*). The nerve-ending of the Chrysomelides seems to present a special point of departure for a physiological reaction which occurs with 1 % osmic acid, and alcohol, or

a process set up by these reagents, before they have had time to affect the muscle-substance itself, the proof being that the lateral contraction corresponding with the nerve-end plate appears immediately before the death of the fibres implicated. Generally speaking, all that has been said of the development of the "fixed" waves applies to the origin of the lateral waves also.

Summing up the preceding observations, the main conclusion is that the cross-striated muscle-fibres of vertebrates, as well as of invertebrates, possess the faculty of conducting long and short, rapidly and slowly transmitted, waves of contraction, which apparently depend upon differences of excitation only. With regard to the normal function of muscles as locomotor organs, the short waves can have but little, if any, significance. This only makes them theoretically the more interesting. The enormous differences in rate of transmission render it at first sight questionable, whether we are really dealing in both cases with the same elements of the muscle-fibres, since no perceptible differences in velocity of conduction have experimentally been found to correspond with the differences of intensity within the range of excitation required to provoke a twitch; nor can the "quick" and "sluggish" muscle-fibres contribute to the explanation, since the differences which they exhibit in rapidity of contraction and conductivity are quite inadequate to explain the disparity. On the other hand, we turn almost involuntarily to the two chief constituents of every muscle-fibre, sarcoplasm and fibrils. We know that in many instances the protoplasm (sarcoplasma) from which the twitching fibrils have been differentiated, is not wholly wanting in intrinsic contractility; many ciliated Infusoria, *e.g.*, have the property through the myoideum, not only of twitching, but also, by contraction of the body-plasma, of making sluggish movements, approximating to the ameboid type. The possibility that the formative plasma of the muscle-fibres in higher animals also may exhibit contractility can the less be doubted, since on many sides (Kühne) the fibrils are regarded as passive, elastic elements, whose main function is the elongation of the muscle. Even if this extreme view cannot be admitted to correspond with the facts, it is equally out of the question to disregard the possibility of contractility in the sarcoplasm. Granting this, however, it would appear from all analogies that the relations between excitability and conductivity in the two elementary constituents

of each muscle-fibre, present fundamental differences, in the sense that the fibrils conduct much more quickly (contract by "twitches"), while the less excitable sarcoplasm, like almost all undifferentiated protoplasm, transmits the excitation-process slowly. On histological grounds it is indeed impossible not to regard the fibrils as co-operating generally in the slow waves of contraction, but it is noticeable that the undulation in the muscle-fibres is best exhibited under just those conditions which have been found experimentally to favour the excitation of non-differentiated, contractile plasma. Mechanical excitation is particularly appropriate, so that, at least in vertebrate muscles, the intensity of excitation must be much greater than is required to provoke a twitch. The time-order of development in the different forms of contraction is also to be noticed, since it occasionally gives an opportunity of observing how the twitch that immediately succeeds, and almost coincides with, the stimulus, is followed by the idio-muscular swelling, from which again proceed the slowly-spreading undulations. This agrees with the much greater latent period and slower development of contraction, in purely plasmatic parts. The question touched on here will only be decided when our knowledge of the functional relations between sarcoplasm and fibrils has advanced much further than at present.

In the cases so far discussed we have been concerned exclusively with conduction of the excitatory process within single, multinuclear, longitudinal cells, such as those of striated, skeletal muscle-fibres. A wave of contraction either stops half-way or spreads to the end of the fibre, from which it can eventually be reflected back, or more frequently expires there. Every tendinous intersection, however small, will entirely block the transmission of even the strongest excitation, so that stimulation of a polymorous muscle at one end only results in contraction of the part directly implicated. It is equally impossible for excitation to be transmitted transversely from one fibre to the next adjacent, and any seeming exceptions (e.g. in drying muscle) are, as we shall see, to be explained on other grounds. The conduction of excitation in muscular organs consisting of uninnuclear muscle-cells is, on the other hand, fundamentally different. Co-ordinated action of a number of muscle-cells in consequence of local stimulation is obviously possible only where the excita-

tion is conveyed by nerves, or where it transmits itself from cell to cell by direct propagation. Both alternatives seem actually to be present.

In the heart, Engelmann (22) was the first to investigate these relations, A. Fick (23) having previously made a short communication on the subject. If a resting frog's ventricle, separated from the auricle, is stimulated at any given point, a general contraction (systole) of the hollow muscle follows, so that the excitation must have been distributed uniformly in all directions from the point of stimulation by conductivity. Engelmann showed that the ventricle need not necessarily be uninjured; the experiment succeeds well if the ventricle of a freshly-killed frog is divided by scissors into two or more pieces, connected only by a minute bridge of muscle-substance; after a time all the pieces will contract successively when any one of them is stimulated. It is quite indifferent at what point each bit is joined to the others, the only essential is that they should be united by muscular substance. The experiment in this form, therefore, indicates "that excitation can be transmitted in the ventricle from any point, to any other point, by any given point." The complete conductivity of the separate muscle bridges, which is disturbed at first, comes back gradually after a certain time has elapsed—perhaps an hour or longer. If a bit of the ventricle is left in connection with the beating auricle, this bit, when conductivity has been fully re-established, will contract first after each auricular systole, then the next, and so on. The contraction is propagated, therefore, in a peristaltic direction from base to apex of the ventricle. If the preparation is no longer beating spontaneously, the succession in which the individual pieces contract will depend only on which piece was first excited, since the contraction proceeds from this successively to all the others; no part is ever omitted. Since we are *a priori* forbidden on histological grounds, as well as from the low velocity of excitation, to assume that each cell is united with its neighbours by nerve-fibres, the second view only is admissible, i.e. that excitation (contraction) proceeds directly from cell to cell in the same manner as within each single cell.

✓ The time-relations of the process of contraction have already been described, in so far as concerns the "twitch" of cardiac muscle. It only remains to consider the rate of conductivity,

i.e. the rapidity with which the excitation is transmitted from section to section. Under normal conditions the velocity is so great in the frog's heart that all points, as in the excitation of striated skeletal muscle, seem to contract simultaneously. This effect may persist in a fresh, vigorous heart, even when the ventricle has been cut up into several pieces. As a rule, however, the undulatory process of the contraction can then at once be recognised. It often seems as though conduction was slower in the bridges than in the larger pieces, for each of the latter seems to contract together, as a whole, while a perceptible time elapses between the contraction of two successive pieces. Engelmann estimated the average rate of conductivity in strips of muscle 10–15 mm. long (snipped out of the ventricle) at about 30 mm. per sec., or more usually 10–20 mm., measured by a metronome, giving beats at $\frac{1}{4}$ secs. Although these values must be considerably below the normal, we may conclude from them that even in the most favourable cases the rate of conductivity must be lower than it is when the excitation is transmitted by nerve. The rate of transmission is diminished to a striking degree by cooling the preparation. Cooling from 17° to 50° C., *e.g.*, is sufficient to reduce it from 20 to 8 mm. Under normal conditions the excitation is invariably transmitted from auricle to ventricle. Engelmann (22) has recently ascertained that muscular conduction is in this case the sole factor, by experiments on the "suspended" frog's heart, arranged on the same principle as that employed by Helmholtz to measure the rapidity with which the excitation of nerve is transmitted. The auricle to some extent represents the nerve, the ventricle the muscle; the former was excited at different distances from the ventricle, and the latent period of the ventricular systole in each case was measured. If conduction was effected by nerve-fibres, the shortness of the strips employed would render any perceptible difference improbable, whereas with cell-conduction in the muscle it was to be expected. As a matter of fact, a very considerable retardation was observed in the commencement of the ventricular systole, when the auricle was excited at a greater distance. In a given case, in which, however, the rapidity was no longer perfectly normal, the delay amounted to 0.09 sec., corresponding to a rate of conductivity of 90 mm. per sec. But this, as Engelmann pointed out, is a value 300 times lower than the

rapidity of transmission in motor frog's nerves under the same conditions. Hence it would appear as if muscular conduction from auricle to ventricle could be as certainly established as within the auricle and ventricle. However much the magnitude of the velocity of muscular excitation may depend on different states of the muscle (fatigue, temperature), it can be maintained under some conditions notwithstanding considerable alterations in the muscle-substance. Thus it would appear that with partial turgescence of the frog's sartorius, the tracts affected may completely lose the power of contracting, without to any extent suffering in regard to electrical sensibility, or conductivity (Biedermann, 24). The same applies, according to Engelmann (*l.c.*), to the muscle bridges of the auricle in the frog's heart, which, "after complete abolition of their contractility, are still able to transmit the motor stimulus to the ventricle, and that with the same rapidity as if the power of contracting was uninjured."¹

It cannot be doubted that the same relations of conductivity of excitation described above for the frog's heart, obtain in the cardiac muscle of higher vertebrates, and this is of the more consequence since there is in general, *e.g.* in mammals, a much less extensive contact of the separate, short, and broad muscle-cells, which really unite only by their blunt end-surfaces and short lateral branches. Similar relations exist, again, in the intestine of insects and myriapods, the walls of which contain anastomosing, striated (uninuclear) muscle-cells, which by contraction set up the normal, peristaltic movements of the digestive tract. Engelmann (25) considers the intestine of the fly to be the most suitable object for combined anatomical and physiological investigation, more particularly the opening of the end of the intestine, from the mouth of the Malpighian tubules to the rectum. "The muscular integument here consists essentially of a single layer of strong, striated circular fibres, enclosed within an unmistakable sarcolemma (invariably absent in cardiac muscle-cells), and separated by perceptible spaces from another." Each fibre seems to be joined to its neighbours by one, or several, oblique or sometimes

¹ Kaiser (*Zeitschr. f. Biologie*, 1894) has recently criticised the cogency of the evidence in these experiments, and refers the effects observed to current diffusion. This can only be ascertained by further experiment, for which we have not yet had opportunity.

transverse branches, by means of which the contractile substance all along the end of the intestine is woven into a physiological continuity. If the last posterior segment of a fly is torn away with forceps, the end of the intestine will usually be left hanging from it, and if examined while fresh in 0.5 % NaCl solution, exhibits lively peristaltic movements: peristaltic waves run every few seconds at tolerably regular intervals from the mouth of the Malpighian tubes towards the rectum. The waves at first spread so quickly that it is impossible to detect the details of the process. But if the preparation is left for a quarter to half an hour, or pressed down with a tolerably heavy cover-glass, the contraction is transmitted more and more slowly, the waves follow at longer intervals, and may be clearly seen to spread themselves over the single fibres and connecting processes. "If, shortly after a wave of contraction has reached the lower end of the opening of the intestine, this end is mechanically stimulated with the point of a needle, an anti-peristaltic wave instantly runs up the fibres of the muscle, to the opening of the Malpighian tubes, if not previously arrested by meeting a wave spreading from above downwards." It is also noticeable that the conductivity of the contractile substance itself appears to be temporarily much depressed by the process of contraction. A wave starting after a long rest spreads with apparently uniform rapidity from its point of departure. But if another wave had immediately preceded it, the new excitation only produces a localised contraction, or at most a wave that quickly diminishes and dies out near its starting-point.

The intestinal tract of some Fishes (*Tench*, *Cobitis*) is well known to contain a similar arrangement of striated muscle-fibres; whether there are analogous relations of conductivity also has not yet been determined (26). On the other hand, the conductivity of the contractile tissues of certain Medusæ (*e.g.* *Aurelia*) has been thoroughly investigated, with results in complete accordance with those yielded by cardiac muscle (27).

The multiform *complexes of smooth muscle-cells* exhibit complete agreement with these mononuclear, striated muscle-cells, in regard to conductivity of excitation. Here, again, it is to Engelmann (28) that we owe the most important conclusions. The ureter of many mammals (rabbit, guinea-pig, rat, etc.) is peculiarly suited to exact investigations, as it offers a delicate

muscular integument, about 1.3 mm. thick in the rabbit, which extends from the hilum of the kidney to the bladder, along the psoas muscle, with a surface of about 11 cm. The muscular sheet, which lies between the adventitia and the mucous membrane, consists of a thin, internal, longitudinal layer, and an external, and much thicker, circular layer. Both are composed of smooth, non-membranous, mononuclear fibre-cells, about 0.2 mm. long, in which hardly any perceptible outline can be detected in the physiologically fresh condition. The muscularis, therefore, gives the impression, even under a high power, of an almost homogeneous, transparent mass. It is only in the moribund condition that fine striæ—the optical expression of the cell-borders—appear between the pale nuclei. Within the connective tissue of the adventitia there is a ramification of nerves, consisting for the most part of pale fibres (Engelmann's "*Grundplexus*"), in which there is a remarkable and complete absence of *nerve-cells*. Engelmann states that the number of nerve-endings within the muscularis is much less than that of the smooth muscle-cells. This point, however, requires further investigation with the recently discovered methods, which would very probably reveal a great abundance of nerves.

As a rule the ureter that has been cautiously exposed exhibits spontaneous waves of contraction, spreading peristaltically at intervals (mostly from 10 to 20 secs.) from the kidney to the bladder. "If a definite point is taken anywhere along the ureter, a weak, momentary dilatation may usually be seen at the segment implicated just before its constriction, after which it becomes thin, cylindrical, and much paler. At the same time the ureter moves perceptibly downwards (towards the bladder). The velocity with which the waves of contraction spread is so low that it can easily be determined. This is effected either by counting the beats of a metronome set at $\frac{1}{3}$ or $\frac{1}{4}$ sec., during the time at which the wave of contraction is transmitted from one point of the ureter to another (one being determined close to the kidney, the other at a more distant spot, by two operators), or they record with a Marey's tambour the contractions of two points remote from one another upon the ureter. With a vigorous rabbit, at sufficiently high temperature, the velocity was 20–30 mm. per sec.; in the cat and rat it appeared somewhat greater" (Engelmann).

With artificial (mechanical) stimulation the contraction is transmitted from both sides of the point excited, while in regard to velocity no perceptible difference between the peristaltic and anti-peristaltic waves can be determined. It is, however, remarkable that *the contraction only appears with direct excitation of the muscularis*. "Neither by pressure of the mucous membrane, or adventitia with the nerve-plexus, nor of the greater nerve-trunks at the hilus and bladder, can a contraction be discharged anywhere in the ureter. Local excitation always produces localised contraction, spreading slowly on both sides. If the ureter is divided, crushed, or tied at any point of its length, a contraction will occur above or below the spot after every excitation, and is transmitted on both sides of the excited part, but never passes beyond the dead point. Since even short excised strips of the ureter react peristaltically when excited, we cannot assume, in view of the structure, that ganglion-cells are responsible for the appearance of the peristalsis; the ureter rather reacts to mechanical excitation in every case "as though it were a single, gigantic, hollow muscle-fibre." We have already seen what an extraordinary influence temperature has upon excitability and conductivity in the ureter, as well as the extraordinary vitality of muscles that are deprived of normal nutrition. Each wave of contraction produces a temporary depression of excitability and conductivity in the sheet of muscle, from which it only recovers during the subsequent diastole and interval (just as in the striated muscle-nets of insect intestine). Every diminution of conductivity expresses itself by the gradual disappearance of the wave of contraction, which, whether spontaneous, or artificially excited, becomes weaker in proportion with the length of its course, and finally dies out even in immediate proximity to the point of excitation. Finally, instead of the advancing wave, there is left only a protracted contraction in the part immediately adjacent to the point of excitation—the analogue of the idio-muscular contraction in striated muscles. The rapidity with which movement is transmitted varies with the conductivity, as is clearly and easily shown by cooling and warming. Since every wave of contraction affects the time-relations of the succeeding wave, it is a matter of course that if the spontaneous contractions succeed one another at irregular periods, those which are preceded by a short pause are transmitted more slowly than those which follow

at a longer interval; as is naturally still more easy to demonstrate with artificially excited waves of contraction. It is evident that immediately after the passage of a wave of contraction, the conductivity is entirely abolished, and only recovers its original proportions a comparatively long time after. In the rabbit the first stage lasts for over a second under normal conditions, and with diminution of excitability may be prolonged to 5, 10, or 15 secs. With normal conditions, normal conductivity is re-established, at most, 10 secs. after the passage of a contraction.

The slowness of the entire process of excitation constitutes an easy and, we may say, direct means of determining the length of the contraction wave in the ureter, if the approximate duration of the contraction is multiplied by its velocity. If we reckon the first at about $\frac{1}{3}$ sec., the other at 33 mm., the wave-length comes out at 1 cm., a value which is tolerably constant, since we find experimentally that the alterations in duration of contraction are, within a wide range, inversely proportional with the simultaneous alterations in the rate of conductivity. These results tally with direct observation, since the length of the contraction wave can be immediately determined on the exposed ureter.

On a ureter that is free from fat and somewhat hyperæmic, it is easily seen that with each contraction a strip of about 1 cm. long becomes pale *in toto*, and progresses in undulations with the constriction. The pallor is generally most marked at the middle of the strip, the ureter sometimes appearing almost white; the normal gray-pink colour then returns by degrees on either side. If anything may be concluded from this as to the magnitude of contraction in the single cross-sections, it would follow that shortening and relaxation of the muscle-substance of the ureter proceed with equal velocity (Engelmann).

It will be seen from the above that a whole series of facts bearing on the relations and conduction of the contraction process may be immediately demonstrated on the part in question, while in striated muscle the finest artificial means have to be employed for their detection—a point which we shall have to insist on later. For the moment we need only refer to the weighty question as to the manner in which the conductivity of excitation (contraction) is effected in the organ—which is composed of innumerable individual cells united by cement-substance.

Seeing that mechanical excitation of the muscular coat produces contraction, when applied to any point of the ureter, which proceeds from either side of the excited spot with a rapidity a thousand times less than the velocity of excitation in nerve; and further, that peristaltic and anti-peristaltic propagation of the movement are exhibited in all parts of the ureter after excision, only one view, as Engelmann stated, is admissible: the peristaltic and anti-peristaltic propagation of the movement is due to the fact that *excitation is transmitted directly from cell to cell in the muscle without intervention of ganglion-cells or nerve-fibres*. In other words: *the ureter in its normal state is physiologically a single, hollow, organic muscle-fibre*. Recent investigations into the anatomical connections of smooth muscle-cells give consistent support to this view, inasmuch as they indicate continuity at least of the sarcoplasm, if not of the fibrils also. But the first is sufficient if, we can hardly doubt, the sarcoplasm can transmit excitation from fibril to fibril. "Plasma bridges" indeed become superfluous, since, as Engelmann correctly observes, there is nothing to prevent such close contact of the naked, sheathless, living fibre-cells, that they form a physiological continuity. This, however, admits that a molecular effect may propagate itself in the ureter *in all directions* from its point of origin. Similarly, of course, we may imagine the process of conductivity within the plexus of the striated muscle-cells. In these parts—consisting of smooth, or striated, uninuclear muscle-cells—we are dealing with an organisation of cells, each individual of which is similarly co-ordinated in function, like the other excitable cell-aggregates of plants and animals with which we are acquainted. Indeed, we are reminded almost involuntarily of the co-ordinated activity of ciliated cells, which can be shown experimentally to stand in close internal relations of conductivity, although the individual elements appear anatomically to be even more distinct than the cells of smooth muscle. Here, at all events, no protoplasmic bridges have been demonstrated, although they unquestionably exist in many smooth muscles, as well as in excitable vegetable-tissues. It appears, however, that in all such cases of "cell-conductivity" the transmission of excitation is much more liable to be disturbed, and is in a much higher degree dependent upon external and internal conditions, than within one and the same cell-body. Doubtless in the last resort this is the reason why

the peristaltic movements of smooth muscular organs, as we know from experiment, are so easily disturbed and affected by a variety of data. This applies in particular, *e.g.*, to the movements of the intestine, which Engelmann treats as analogous with the peristalsis of the ureter (29). Apart from the richly-developed plexuses of nerves and ganglia in the wall of the intestine, and its far more complex development of muscular layers, the structure of the two organs shows such a fundamental agreement that we are justified in assuming *a priori* that the conductivity of excitation and contingent peristalsis are derived in both cases from the same principle. In this connection we have especially weighty evidence in the fact that a wave of contraction starting from any point in the continuity of the intestine is transmitted under favourable conditions to either side of the point of excitation, just as it is in the integument of the ureter, *i.e.* peristaltically and anti-peristaltically. This is not, indeed, the case invariably—nor, above all, in every animal. Thus in the frog's intestine, even under the most favourable conditions of excitability (in summer with a high temperature), local excitation will scarcely ever produce anything more than localised constriction, or at most spreading over a few millimeters. The reaction is much more easily provoked on the living, warm-blooded intestine, *e.g.*, of cat or dog, which has the further advantage that on opening the abdomen the intestines are usually quiescent, which is not to the same degree the case with the rabbit. But even here the observations required are not nearly so certain as in the ureter. It would rather seem as though a certain condition of excitability in the intestine was essential to the success of the experiment. According to Engelmann this is best secured when the animal is killed by bleeding from the large cervical vessels. If the belly is opened soon after the last respiration, the intestines are either in the required state, or pass into it shortly after. If the muscular coat of a loop of the small intestine is then mechanically excited at any point (by pinching with forceps), Engelmann finds a vigorous contraction of the circular layer of fibres, which spreads outwards from the excited spot in a peristaltic and anti-peristaltic direction over the whole small intestine, at a low velocity of about 40 mm. per sec. Engelmann gets the same results with excitation of the large intestine. While at the first stimulus the contraction is pronounced throughout its entire

course, it exhibits later on an increasing diminution and retardation of the wave, in proportion with the distance from the starting-point, until finally only a local constriction remains visible.

The reaction of the intestine is thus in complete conformity with that of the ureter. As Engelmann has made analogous observations upon the stomach and intestine of rats, mice, pigeons (most elegant), the oesophagus, stomach, and intestine of frog, and uterus and vagina of pregnant rabbits, the conclusion may be accepted that in all cases in which peristaltic movements can be provoked, anti-peristaltic contraction is also at least possible. It must be admitted, on the other hand, that conductivity of excitation within the muscular coat of the intestine is frequently absent, when it might more reasonably be expected. This occurs more particularly when the abdominal cavity is opened in warm salt solution, when the intestine usually remains perfectly quiescent. If under these *approximately normal* conditions any point is stimulated mechanically by gentle pressure, or ligature, only a local, circular constriction will appear (as stated by van Braam-Honckgeest (30) and confirmed by Nothnagel (31)), which is confined to the seat of excitation, and never spreads beyond it in a peristaltic or anti-peristaltic wave of progression. As there is no reason to suppose that conductivity is lower here than after bleeding the animal, from Engelmann's point of view no other assumption is possible, but that the transmission of excitation is blocked by a kind of inhibition, possibly proceeding from the ganglionic plexus. And, experimentally, it is impossible to deny the co-operation of nervous impulses, whether of an inhibitory or motor nature, in intestinal peristalsis. The question then arises whether the normal movements, *i.e.* the propagation of a wave of contraction in one or the other direction, may not be produced, in each point of the area traversed, by a nervous impulse. It can, indeed, hardly be disputed that such impulses must play a very important part in the discharge of the contractions which usually follow in rapid succession. The extreme slowness of transmission, which may be followed with the eye, can, as already pointed out by Engelmann for the ureter, be urged against the first view. On the other hand, it affords no better explanation than Engelmann's theory of the localisation of excitation effects in the perfectly normal intestine, or the sudden extinction of a wave of contraction, as, *e.g.*, often observed by Nothnagel (*l.c.* p. 14).

Perhaps the soundest hypothesis is that propagation of a peristaltic wave does under all circumstances depend upon muscular conductivity, but that the discharge of excitation, as also the inhibitory processes which may become effective at any point, are governed by the nervous organisation in the wall of the intestine. This view is in ultimate agreement with the striking effects—observed by Nothnagel—in chemical excitation of the intestine with salts of sodium and potassium. Unfortunately it is not possible to test the hypothesis in question by putting the ganglion-plexus functionally out of court with specific poisons; but the effect of small doses of ether and chloroform might be investigated, since it may be supposed that the ganglion-plexus loses its excitability earlier than the intrinsic muscle-elements. The possible discharge of peristaltic and anti-peristaltic waves at a certain stage of death from hæmorrhage may perhaps also depend on an earlier loss of vitality of the intestinal ganglia.

In conclusion, it may be said that conductivity of excitation in smooth, muscular organs is rarely obvious and certain; in the majority of cases it is wanting altogether. The formation of an “idio-muscular” swelling contraction at the seat of excitation, which only disappears very slowly, is the rule with localised excitation.

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CHAPTER III

ELECTRICAL EXCITATION OF MUSCLE

THE electrical current undoubtedly ranks first among all the artificial stimuli of irritable substances at our command. And this not merely on account of its easy application, and the possibility of measuring its intensity by the finest gradations, but above all in regard to the specific nature of its action.

Whenever the electrical current has been referred to as an excitation in the preceding observations, it signified almost exclusively single, or rapidly repeated, induction shocks, the primary object being to produce a momentary stimulus, easily varied in strength, which should injure the excitable portions as little as possible. But, on the other hand, the more exact investigation of the manifestations of excitation produced by the *constant current* in muscle is of great interest, and of the highest importance in estimating the mode of action of the electrical current. As regards the *technique* of the experiments, some preliminary observations on method are advisable. In all the earlier experiments on animal tissues in which the electrical current served as a means of excitation, the excitable parts were stretched over convenient metal electrodes, usually made of platinum, by means of which the current was led into them. The value of this method was, however, much diminished by the polarisation current invariably associated with it, so that it became a *sine quâ non* under all conditions, to employ non-polarisable electrodes whenever constant currents were made use of—still more so with strong currents and prolonged closure. Ever since du Bois-Reymond enlarged the *technique* of electro-physiology by the invention of his unpolarisable combination of amalgamated zinc and zinc sulphate, in order to lead off currents of animal electricity, these electrodes have

found the widest application in excitation experiments, several different forms having been adopted. When it is required to lead a current into a striated muscle, the shifting of the contracting muscle under the electrodes in contact with it is a ready source of fallacy, which can only be avoided where the electrodes are fixed to the muscle, or bones into which it is inserted, so as to follow every movement. Hering was the first to construct non-polarisable, shifting electrodes for the frog's sartorius, which, from its regular structure of parallel fibres, is singularly appropriate to such experiments, and is easily prepared without disturbing its natural relations with the bones of the leg and pelvis :

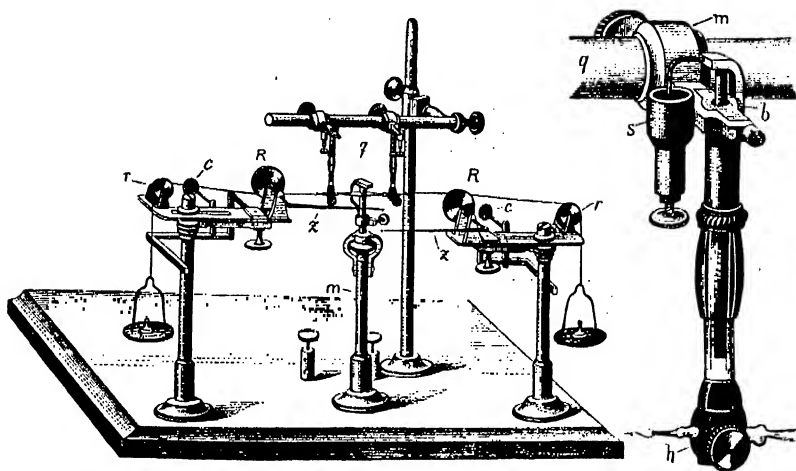


FIG. 71.—Apparatus for investigating the polar effects of the electrical current in muscle (double myograph). A non-polarisable movable electrode. (Hering.)

these electrodes serve for a variety of purposes (1). "A 5.5 cm. glass tube (Fig. 71) is provided at the upper end with a split brass holder, carrying two diametrically opposite points, which fit into the holes of a pivot, so that the vertically dependent tube may easily turn on the points, and oscillate from them. The pivot is fixed to a brass ring (*m*), which can be moved along a horizontal rod (*q*) of bone or ebonite. A short ebonite cylinder (*h*) is pushed over the lower end of the glass tube, the opening of which is the continuation of the bore of the tube, and is transversely pierced in such a way that a slender bone like the tibia or os ileum of the frog can be passed through the hole, and fixed by a screw. A small amalgamated zinc rod is dropped into the tube from above,

and supported by a brass stirrup fixed to its upper end, which again is attached to the brass holder of the tube. This stirrup is continued on the other side as a short, copper wire bent downwards to dip into a steel cup filled with mercury (s). As the rod swings to and fro, contact is made between the end of the wire and the mercury. At the lower end of the pool is a terminal to which the wire is fixed. When in use, the ebonite collar and bottom of the glass tube are filled with salt clay, the upper part with solution of zinc sulphate, with the zinc rod dipping into it. After the bone has been pushed through the orifice of the ebonite collar into the clay, it is fixed by the screw. The bone at the other end of the muscle is similarly fixed, so that the muscle is now horizontally stretched between the two electrodes. Further, a thread is attached to the lower part of each electrode, connecting it with a muscle pointer. Either of the electrodes can be fixed, leaving the other to follow the shortening of the muscle."

Assuming that the electrode of the pelvic bone is fixed, the movement, or change of form, of the whole muscle can easily be observed and graphically recorded, if the other free electrode is connected with a long pointer (z), by a thread running horizontally over two pulleys (R and r , Fig. 71) with a weight at the end of it, the pointer again being attached to the axis of the larger pulley. Since the writing-point naturally describes an arc of a circle, the curve of contraction on the smoked surface is more or less distorted, which, however, matters little in the present consideration. If under these conditions the effect of varying strengths of the constant current is investigated upon a curarised (denervated) sartorius, it is easy to see that under the most favourable conditions of excitability in the muscle, permanent closure of a weak current never provokes more than a single brief "twitch," which is at first insignificant in height, but rapidly attains its maximal value, if the current increases in intensity.

Beyond a certain limit of intensity the height of the make twitch remains constant; other changes, however, appear in the curve to which we shall refer later. On comparing the maximal twitches produced by single induction shocks with the maximal "make twitches" of the constant current under uniform conditions, we are at once struck by the much greater height, as well as the blunt, rounded top, of the latter. This can be

detected even at a slow rate of the recording surface, but is much plainer with a quick movement. According to Tigerstedt (2) the process of each make contraction must be of a tetanic character, since the corresponding curves are much more extended than in twitches provoked by induction currents (Fig. 72). But it is needless to say that there is not necessarily any true "tetanus," i.e. contraction resulting from summation. From these facts alone we may conclude that besides the *intensity* of current, its *duration* in the muscle also affects the strength of excitation (or contraction), while this appears yet more plainly from corresponding experiments on sluggish muscles,

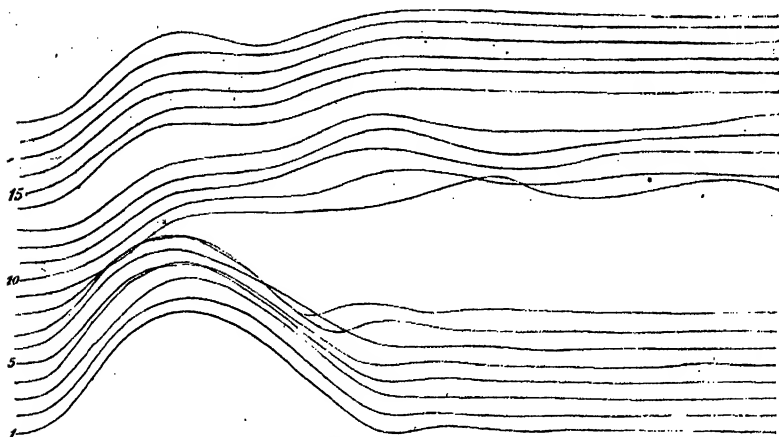


FIG. 72.—1-8, Contraction curves on excitation of the muscle by single induction shocks; 9-19, contraction curves (make twitches) on exciting with the constant current ("tetanus" character). (Tigerstedt.)

where the magnitude of effect as dependent upon the duration of the excitation appears to be in exact inverse ratio with the mobility of the particles of an irritable substance. The extraordinarily small and often negative effect of single induction shocks on many protozoa, and on vegetable protoplasm, is well known, while in smooth muscle such short stimuli, if they act at all, first take effect at a high intensity, although they seldom or never fail to excite the rapidly twitching striated fibres. This is remarkably well seen on every relaxed (a-tonic) preparation from the adductor muscles of anodonta (3). From these, as was said above, it is easy to obtain a preparation as susceptible to electrical excitation as the frog's sartorius (Fig. 73).

Then, after permanently fixing one half of the shell, non-polarisable brush electrodes can be applied on both sides, as near as possible to the insertion of the muscular band (which usually consists of parallel fibres), while, in order to prevent any shifting of the electrode corresponding with the other movable half of the shell, the current at this point is best led in by a short loop of thread.

If a current of adequate strength is then sent through the relaxed muscle, changes of form may be observed which, apart from the sluggishness of reaction more or less characteristic of all smooth muscle, concur on the whole with those exhibited by striated muscle under analogous conditions. As regards form

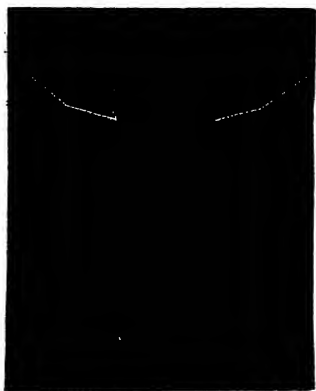


FIG. 73.—Schema of electrical excitation in adductor muscle of molluscs.

and process of contraction during closure of the current, the resulting curve will of course rarely correspond with the process designated *in* *re* the time-distribution of the contractions of striated muscle, the "make twitch." Apart from the slowness with which the whole process occurs, the difference of duration between the contraction and relaxation phases (periods of rising and falling energy) is much more marked in smooth molluscan muscle, which gives a distinct and peculiar character to its curve of contraction. Two cases

must here be distinguished, that in which the current is opened before, or as soon as, the muscle has reached its maximum of shortening, and that in which there is a long period of closure. In the first case, at least under certain conditions, *e.g.* with warmed and therefore quickly reacting preparations, curves are obtained, which from their form and process might be regarded as extended twitch curves, since not only does the shortening rapidly rise to a considerable height, but the relaxation also occupies a comparatively short time (Fig. 74).

In other cases a longer closure of the circuit produces curves which rise abruptly at the moment of closure, without sinking down again, corresponding with a persistent and uniform shortening of the muscle. Under these conditions the closure

may last a minute, and the muscle remain nearly as long in a state of maximal shortening,—when excited by weak as well as by strong currents. The dependence of contraction magni-

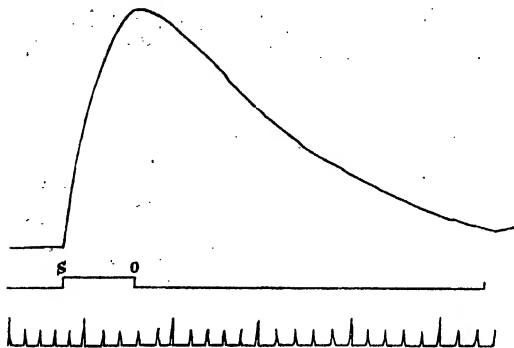


FIG. 74.—Closure contraction of adductor muscle of *Anodonta* (excitation by the constant current); (s), closure; (o), opening.

tude on duration of closure is most plainly seen on the preparation in question if the circuit is opened *before the maximum of shortening is reached*. Constant currents which produce maximal contraction of the muscle when closed for 3–4 secs. often effect a merely insignificant shortening if closed for only $\frac{1}{4}$ sec. At this range the closure contraction is greater with unaltered

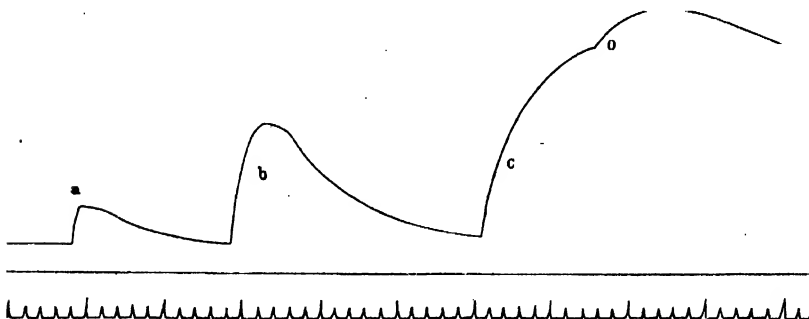


FIG. 75.—Effect of duration of current on contraction magnitude of adductor muscle of *Anodonta* (excitation with constant current); (c), duration of closure = $\frac{1}{4}$ sec.; (b), = 1 sec.; (a), = 4 secs.; (o), opening contraction. (Biedermann.)

strength of current in proportion with the time during which current passes (Fig. 75). This agrees with the fact that single induction shocks only stimulate the most excitable preparations at a very high intensity, so far as may be concluded from the visible

changes of form (Fig. 76). Fresh muscles, or those which, though older, are still in a state of considerable tonic contraction, generally appear quite insensible to induced currents.

The advantages of a sustained passage of current over brief "current impacts" is also seen in *tetanisng excitation periodically repeated*. Fick pointed out that the rapid make and break, by hand, of an intrinsically effective constant current, generally failed to excite smooth molluscan muscle—yet the duration of the single impacts here is considerable; if it is still further lessened, stronger and stronger currents will be required to produce any excitation. This is especially striking in excitation with a rapid succession of induced alternating currents, and Fick states "that in the same circuit that closes the secondary coil of an ordinary induction apparatus, a frog's muscle may fall into the most lively tetanus, while the molluscan muscle shows no sign of excitation," and that this even occurs with currents

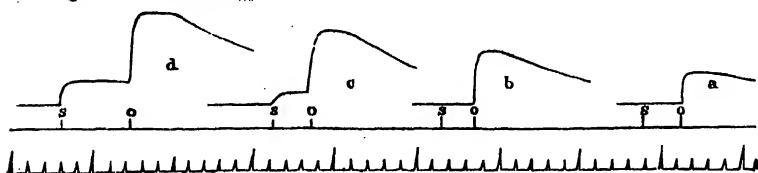


FIG. 76.—Contraction curves of adductor muscle of *Anodonta*, excited by single make and break induction currents (s and o) of increasing strength (a, at greatest distance of coil).

that are strong enough to throw the muscles of the experimenter's hand into tetanus (4).

Engelmann's observations on the ureter (5) naturally fall into line with these experiments on the smooth adductor muscle of molluscs. Here, too, it is easy to demonstrate that the make contraction occurs only when the duration of current exceeds a certain limit, which is lower in proportion with the strength of the current. This is plain from the accompanying table (Engelmann).

Strength of current in rheochord resistance.	Minimum closure, required to produce contraction.
4000 cm.	< $\frac{1}{3}$ quarter second.
500 "	$\frac{1}{2}$ "
50 "	1 "
25 "	2 "
15 "	3 "
12 "	4 "
11 "	
10.5 ..	

In conformity with this, "powerful intensities" of current are required to produce contraction of the ureter by single induction currents. Engelmann was the first to accomplish this by taking metallic electrodes (zinc wires), shortening the intrapolar tract, and connecting the primary coil of du Bois' induction apparatus with 2-4 Grove cells.

We have repeatedly stated that effects which can only be determined in voluntary muscle by complicated methods and the finest instruments, can be observed directly in smooth muscle. This also applies in a marked degree to the effect of *duration of current* upon excitation. It was shown above that the marked difference in the height of maximum twitches, according as excitation is with the induced or the constant current, is a sign that duration of current is in the last case an intrinsic factor. Fick was the first to establish exact data *re* constant currents of uniform intensity and varying duration, for striated frog's muscle. This is much harder than in smooth muscle, since, as might be presumed, the time during which current must pass in order to produce a true excitation is much shorter in striated muscle. And in fact in experiments where closure has been effected by means of an ordinary key, there is never any perceptible effect of duration of current on the height (magnitude) of the twitch at closure, as may be readily understood. If current once lasts long enough for the muscle to reach its maximum of contraction, the closure twitch cannot be affected by any further duration. And this must more especially be the case when the circuit is opened and closed, however quickly, by the hand of the operator.

Under certain conditions striated skeletal muscle also becomes modified, so that the relative inefficacy of very short stimuli is exhibited, without any particular refinement of instruments. Brücke found that the sensibility of striated muscle to short currents diminished when it was curarised. It has long been known in clinical medicine that paralysed striated muscles exhibit a certain inability to react to short, induced currents, although their relation to variations of the constant current is perfectly normal, and this has been the basis of a great number of investigations (6). Erb (*l.c.*), for instance, found in paralysis, such as Bell's palsy in rheumatism, or by section of the nerve, that the sensibility of the muscle to short currents was diminished, or

completely abolished, while it was fully maintained and even heightened for the constant current. Neumann observed similar changes in fatigued or moribund conditions.

Along with these changes there is the gradual development of a much more sluggish process of contraction, so that here too contractile substances with a slow reaction require a longer period of excitation than those which react quickly. This is developed to such an extreme degree in many smooth muscles, that one is justified in saying that moribund striated muscle, especially at the beginning of degeneration, approximates to a certain extent, in its physiological properties, to smooth muscle. The differences described are most marked in a series of observations (not yet published), by T. Krehl (Jena), on frogs, in which one sciatic nerve had been divided at the thigh. After $\frac{3}{4}$ year the comparison of the two gastrocnemii still exhibited marked differences on excitation with tetanising, or single, induction currents, or, on the other hand, with the constant current. In the first case the coil had almost to be pushed home before the slightest effect could be produced in the paralysed muscle; in the second an excessively marked, persistent contraction was exhibited during closure. The muscle of the uninjured side reacted normally.

A. Fick (7) was the first to show by unexceptionable experiments, that the make excitation is a function of duration of current in this case also. In order to regulate the duration of a single "impact of current" as required, Fick used a spring-contact, which conducted a metal point rapidly over a metallic plate of varying breadth (spiral rheotome). From this it appeared that, with excitation of a normal striated frog's muscle, the magnitude (height) of twitch produced by closure of the constant current depended not merely on strength of current, but on the time during which, at constant density, it was passing through the muscle. The limit below which the duration of closure must not fall, if the height of twitch is to remain maximal, corresponds according to Fick with about 0.001 sec. Even if this value is only approximate it shows that the difference between the duration of closure required to produce an effective make excitation in smooth muscle, and in striated frog's muscle, is enormous. We shall see later that a similarly graduated difference also occurs between striated muscle and medullated nerve,

a still shorter duration of closure being sufficient to excite the latter.

Summing up the results of the preceding observations, we may say that under all conditions a current of given strength must traverse the muscle for a perceptible time, in order to bring it from a state of rest into that of maximal excitation, corresponding with the intensity of the same current. If the cause of excitation, *i.e.* the current, acts for too short a time, a weak contraction only will ensue, because the new state cannot develop itself fully; with still shorter duration of current, the effect is altogether wanting, because the stimulus does not act long enough to induce in any perceptible degree those changes in the muscular substance which are the fundamental cause of contraction. The time required varies within a very wide range in different muscles with quick reaction, but is, generally speaking, greater, as the period of contraction is more sluggish.

If we may conclude from the above that the excitatory process is caused by the current, not merely at the moment of its commencement, but *also during its passage*, this is still more certain from a closer investigation of the changes of form in a muscle *during persistent closure of current*. We have already pointed out in smooth molluscan muscle that it may, under these conditions, remain as long as a minute in unbroken, persistent contraction. The magnitude of this "persistent closure contraction" increases up to a certain limit with the strength of the exciting current, but the effect *per se* is quite evident at all working grades of intensity; indeed, it may be said that the persistent closure contraction is, generally speaking, the single form of contraction in smooth molluscan muscle that corresponds with persistent closure. If the reaction of striated muscle is compared under the same conditions, there are noticeable differences. We have already found that below a certain limit of current intensity a single "twitch" is alone provoked at closure, the muscle shortening rapidly, and elongating again almost as quickly, even when the circuit remains closed. When in any given case the closure twitch has reached its maximum, a further increase of current intensity produces no increment in height of contraction, but there are certain changes in the form of the contraction curve, which express the persistent shrinking of the muscle during the entire passage of the current.

Wundt (8) was the first to observe that the muscle does not recover its normal length immediately after the closure twitch has subsided, but exhibits a greater or less degree of shortening, which only relaxes suddenly and sharply when the circuit is opened, provided this break does not in itself excite the muscle and produce a vigorous second contraction (opening twitch). The magnitude of the persistent closure contraction increases in this case also, up to a certain point, with the strength of the exciting current; it is—at any rate under the given conditions—(recording the changes of form with Hering's double myograph) imperceptible with weak currents, but expresses itself plainly later on in a specific section of the curve, inasmuch as the descending shoulder of the curve does not reach the abscissa, but runs along more or less above it, so long as the current remains closed (Fig. 77, K).

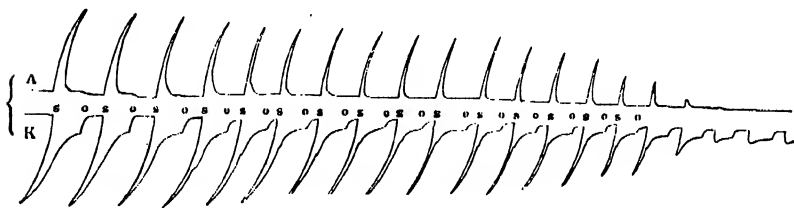


FIG. 77.—Sartorius fixed in the middle (double myograph). Successive excitations at closure with uniform strength and direction of current. Effect of (local) fatigue at the kathode.

With the application of very strong currents, the make twitch eventually appears only like a hook, since the muscle relaxes very little after reaching its maximum of shortening, thus approximating to the normal reaction of smooth molluscan muscle. This seems to appear earlier, and to be more marked, in preparations that are already fatigued, and less capable of reacting. The persistent closure contraction is in general capable of much greater resistance than the closure twitch, as appears *inter alia* from the fact that when a muscle is fatigued by repeated closure with unaltered direction of current, the initial twitch rapidly diminishes in size, and at last ceases to appear altogether, while the persistent contraction decreases only very slowly with progressive fatigue of the muscle. The initial twitch has long disappeared, when each new closure still excites the muscle to persistent shortening in almost the same degree as at the beginning of the experiment (Fig. 77, K); it is not

till much later that this effect also vanishes. In every such case striated muscle then reacts from the beginning exactly like smooth molluscan muscle; there is, as a rule, no twitch at closure, only a more or less considerable sustained contraction, so that in this particular also there is agreement between fatigued striated and normal smooth muscle. Taken in conjunction with previous evidence, the persistent closure contraction shows indisputably that the electrical current sets up a process of excitation in striated, as in smooth, muscle, throughout the duration of its passage.

The effect of duration of current is even more striking in the *opening excitation* than at closure, so that the influence of current intensity is relatively at a discount. With low current intensity, and short duration of closure, there will be no opening excitation; currents to the closure of which a curarised muscle responds with maximal twitches and strong sustained contraction, often provoke no trace of visible excitation when they are broken, or in the most favourable cases a weak opening twitch may occur after *prolonged* closure only. Although, on the other hand, strong currents will often effect an obvious break excitation after even a short closure, it is not primarily the *intensity of the current* which causes the break effect, but the duration of its passage. The same alterations as may be observed in the curve of the closure contraction with increasing intensity of current, appear again in the curve of the opening contraction, if the passage of current which precedes it has been of long enough duration (24).

The simplest change of form with which a striated muscle reacts to the opening excitation is again a (break) *twitch*; contraction occurs quickly at the moment the circuit is opened, and the muscle almost as quickly returns to its normal resting proportions, so that curves are produced analogous to those of the closure of weaker currents. But the opening twitch only occurs in this simple form when the muscle is highly excitable, the current not too strong, and the duration of closure not unduly lengthened. Strong currents almost regularly produce more or less extended (tetanic) opening twitches, which always appear to be antagonistic to the previous persistent closure contraction, since the ascending shoulder of the curve rises from the line of the persistent contraction as its abscissa, while the descending portion drops to the original abscissa line (Fig. 78).

If a strong current is kept closed until every trace of persistent shortening has vanished, the muscle will not resume its natural length directly the break twitch has expired, but remains *persistently* shortened ("persistent opening contraction"); the closure of a homodromous current in this case produces not a shortening, but an elongation of the muscle; it is easy to show that not merely the height of the opening twitch, but the magnitude of the persistent opening contraction also, increase up to a certain limit with the duration of the previous passage of current. The twitch entirely fails to appear, both at closure and opening, with diminished excitability of the muscle, and only the persistent contraction marks the effects of excitation. The muscle then shortens when the current is opened, remains contracted for some time, and lengthens instantaneously

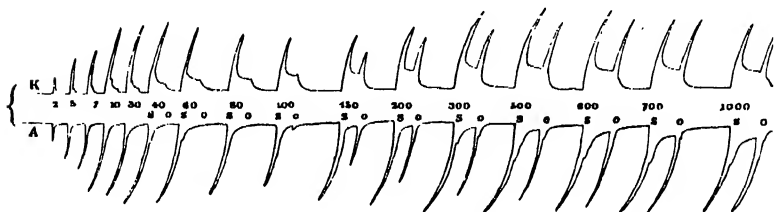


FIG. 78.—Series of curves of twitches from the sartorius, fixed by its belly, in the double myograph. K, Kathodic; A, anodic half. The figures correspond with the rheochord resistance. Effect of increasing strength of current (s, closure; o, opening).

upon closure of the homodromous current. Thus, as regards striated muscle, three chief forms of contraction may be distinguished at the opening as at the closing excitation: (i) the simple twitch, (ii) twitch immediately followed by persistent shortening, (iii) persistent contraction without previous twitch. Of these, (i) corresponds with the weakest degree of excitation, (iii) is a fatigue effect. It is evident that Wundt studied only the third form in his experiments on the opening excitation; i.e. he says: "If the circuit is closed for a long period, contraction will follow upon breaking it; this occurs much more slowly than contraction in a twitch; it remains some time at its maximum, and only gradually gives way to elongation" (8, p. 142). Against this it must be observed that even when the current has been passing for hours, a definite twitch will follow on breaking it, provided that excitability and conductivity are preserved as far as possible.

Since the sluggish, smooth muscles do not yield any *twitch*, it is self-evident that at break, as at make, of a constant current, the change of form will always correspond in character with the more or less pronounced *persistent contraction* only. If experiments are tried with the adductor muscle of anodonta, when free of tonus, and as relaxed as possible, somewhat strong currents, and a long closure, will be required to produce a distinct opening contraction, the curve of which then appears superposed upon the curve of the closure contraction—near its summit—in consequence of the slow relaxation of the muscle (Fig. 75, *o*). On the ureter of the rabbit also, Engelmann ascertained that in order to produce a break contraction, the closure must exceed a certain duration. It is arrived at earlier with strong than with weak currents, in proportion with the increase of excitability. "With greater strength of current, and higher excitability, an opening contraction may occur even after a closure of less than $\frac{1}{4}$ sec.; with currents of lower intensity, and with diminished excitability, a closure of 30--60 secs. is not seldom required." For the rest—given the same current, and a certain degree of excitability—the total duration of the break contraction increases up to a certain limit, with increasing duration of closure. Accordingly, both on opening and on closing the constant current, a *persistent* excitation will be produced, not merely in smooth muscle, but in striated muscle also, the magnitude of which depends, in the first case, mainly on current intensity, while in the second it is also to a considerable degree dependent upon the duration of passage of the current.

The reaction of smooth molluscan muscle that has shortened at a certain degree of tonus, is quite characteristic with regard to the appearance of the break excitation. We have already seen that in each such case the closure of a battery current, if effective at all, produces only a very weak excitation. As the break stimulus, both in striated and in smooth muscle (free of tonus), always produces a much smaller effect than the make stimulus under the same conditions, it is very striking that the first visible effect of excitation upon a fresh, highly "tonic," preparation of molluscan muscle should occur without exception on opening the circuit only; while its closure either produces no effect, or a shortening that is minimal in comparison with the opening contraction (Fig. 79, *a*). Even when the intensity of a just effective

current is considerably increased in the sequel, no essential change can be observed in the response of the muscle, unless it be that the opening contraction then appears vigorously after only a short duration of closure. With any effective intensity of current a period of 1–2 secs. is usually sufficient to cause perceptible shortening of the muscle; but the effect increases within certain limits, if the closure is lengthened with unaltered direction and intensity of current. It is to be noticed that the magnitude of the break contraction diminishes very rapidly with repeated excitation of the same preparation; this seems to coincide with the extremely slow subsidence of all excitation phenomena, and thus of the persistent opening con-

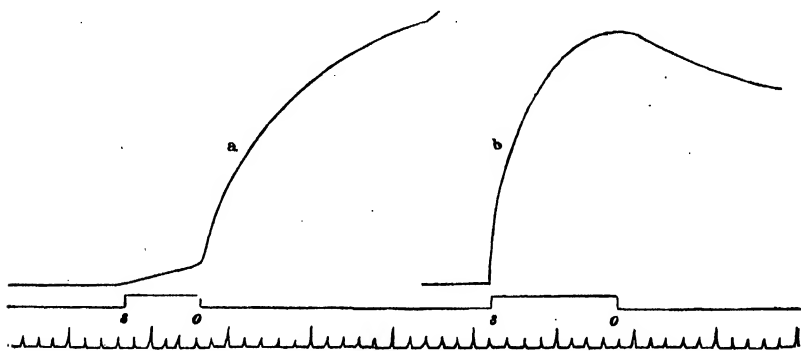


FIG. 79.—Contraction curve of adductor muscle of *Anodonta* on excitation with the constant current. *a*, Immediately after preparation (pronounced tonus); *b*, 4 hours later, after relaxation of the muscle; (*s*), closure; (*o*), opening of current.

traction also, since it is minutes before, at uniform loading, the shortened muscle resumes its original proportions. Under these conditions it is obvious that only in a very limited sense can there be any comparison of the results of repeated excitation of one and the same muscle under rapidly alternating experimental conditions (*e.g.* differences of closure and current intensity), since from the extreme slowness of relaxation the first experiment alone can, as a rule, be taken into consideration. We may assume that other smooth muscles with a developed "tonus" will react in the same way towards galvanic currents as the preparation in question. Morgen (9) experimented with a circular piece of frog's stomach, which was suspended between two metal hooks in a moist chamber while still connected with the mucosa or after freeing it of the latter, so that the changes

of form in the ring of muscle, which was suitably loaded, could be recorded by the graphic method. On exciting the preparation with the constant current a marked difference appeared, according as the mucosa was present or absent. In the first case contractions occurred plainly both on closing and on opening the circuit; but as excitability diminished in preparations that exhibited a certain degree of tonus, the break excitation became more and more prominent—its magnitude moreover increasing within a certain range with the duration of closure. After a very long latent period (usually of several seconds) the contraction began so slowly, that the maximum was usually reached after half a minute only. Relaxation then set in immediately, proceeding as or even more sluggishly. After removing the mucous membrane, Morgen noticed that the closure contraction, as a rule, failed altogether, and only the opening of the circuit was followed by a marked shortening. The same preparation exhibited an analogous reaction when the animal had been poisoned with morphia. It seems highly improbable that the occurrence of the make contraction should in this case be associated with nervous elements (ganglion-cells). It must essentially be an effect of the tonic contraction of the muscular coat, increased by preparation. Bernstein, under whose direction Morgen's investigation was carried out, remarks further that preparations which exhibit frequent and well-marked spontaneous contractions also give very pronounced contractions at closure, while this is not the case with non-excitabile or narcotised preparations.

It has already been stated that electrical stimuli that are ineffective *per se*, are, if repeated frequently at a sufficient interval, readily summated into an efficient excitation, and Engelmann (*l.c.* p. 282) established the same fact for closing, as well as for opening stimulation of the rabbit's ureter. The latter also occurs under certain conditions in the smooth muscle of molluscs (Fig. 80). On applying stronger currents, a new and further shortening is seen to occur (especially in preparations not wholly relaxed) after prolonged rhythmical excitation. There can be no doubt that this is an opening contraction, which must be explained by the summation of intrinsically ineffective break stimuli, as already pointed out by Fick in the same connection (4, p. 44 and p. 50). We have no hesitation in recognising in

this effect the analogue of that "final twitch," which, as we have shown, sometimes appears at the end of tetanising excitation of striated muscle with very frequent induced currents, just as the "initial twitch" must be regarded, under the same conditions, as analogous to the closure twitch on excitation with the constant current.

A fundamental distinction between the "twitches" produced by single induction shocks and by the closure or opening of the constant current is, as we have already pointed out, the more extended curve ("tetanic character") of the latter. The entire process of shortening is prolonged in all its individual phases (but especially in the stage of falling energy), in correspondence

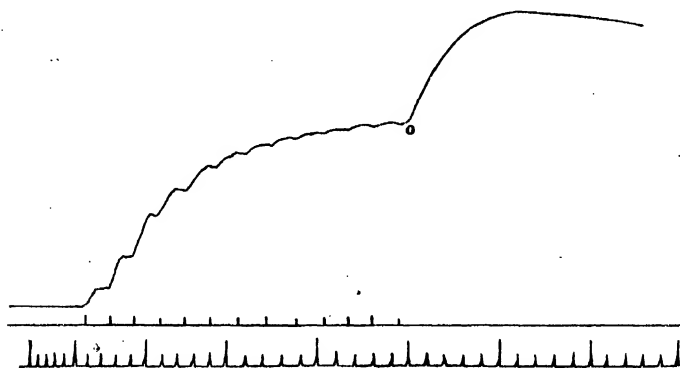


FIG. 80.—Opening contraction (o) of adductor muscles of mollusc (*Anodonta*) after rhythmical excitation with a strong constant current (10 Dan.). Incomplete tetanus during excitation. Time-tracing in seconds.

with the greater duration of the make or break excitation. The relations of the latent period in both cases is a point of great theoretical interest. We owe its thorough investigation to Tigerstedt (2), v. Bezold (10) having previously ascertained that the make twitch, with not unduly strong currents, has a shorter latent period than the make induction twitch. The difference according to Tigerstedt (in the non-curarised gastrocnemius) is on an average 0.003 sec. We have invariably observed the same results in experiments (to be described below) on the curarised sartorius. In excitation with the constant current the magnitude of the latent period, as shown by v. Bezold, depends essentially upon current intensity, the more so in proportion as the current used for excitation is weaker. If the intensity of

current is much increased, the effect on the latent period, though pronounced at first, may disappear completely. In the opening excitation the latent period, is as a rule, longer than at closure, so that with weaker battery currents the difference, as compared with induction twitches, is even more marked than at closure. But with increased current intensity and prolonged closure, it may be almost entirely abolished in this case also. In inquiring into the cause of the shorter latent period in make and break induction twitches, the answer comes to hand when we remember that in order to provoke a "twitch," a certain acceleration of increase in the intensity of current in the muscle is essential. According to the law proposed by du Bois-Reymond, the electrical current does not excite by its absolute density, but by its relative changes from one moment to another, the incentive to movement consequent on these changes being the more considerable in proportion with their rapidity at uniform magnitude, or brief duration in a time-unit.

And if, on the other hand, we have reason to suppose that constant currents of medium strength undergo slower alterations of density within the muscle than induction currents (in consequence of lower potential), then the longer latent period, at least for closure twitches, would, as Tigerstedt points out (*l.c.* p. 197), be dependent upon purely physical factors, and the self-evident consequence of du Bois-Reymond's "general law," as above stated. But we have already shown that the first half at least of this law has no application to muscle, and we shall subsequently find that the second half is not generally applicable either. This does not indeed cancel the possibility of explaining the above differences in the latent period as indicated.

Here, we are obviously dealing with the commencement of the contraction only, not with its final magnitude and further process. Although the excitatory effect of short, induced currents is certainly less than that of battery currents so far as regards magnitude and duration of the twitch, it is easy to show that the degree of current density required to produce a twitch, however small, is more easily arrived at with induced, than with constant, currents.

This leads us directly to the question of the dependence of excitatory effects upon the distribution in time of the electrical movement. On comparing contractile substances collectively, we are

met by the significant fact that rapid variations of density in a current are an effective stimulus to highly mobile kinds of protoplasm (striated muscles), while they are ineffective towards more sluggish portions. This is clearly shown by the fact that normal striated muscle, when excited with the constant current, twitches conspicuously at the moment of appearance and disappearance (closure and opening) of the current. *The visible manifestations of persistent excitation fall into the background, while the excitatory effects of current variation come prominently forward, in proportion as the excitable protoplasm is more highly mobile.* This dictum is sufficiently borne out by the total results of experiments on contractile substance. It finds characteristic illustration when the action of a *gradually* increasing current on different irritable tissues is examined. If the circuit is closed as usual by hand, *e.g.* with a wire dipping into mercury, the intensity naturally rises with excessive rapidity from zero to its maximum, so that the form of the curve of variation is unrecognisable in detail. But by using a contrivance, by means of which the intensity of the current can be gradually increased from zero—as in the slow and uniform gradation of the slider in du Bois' rheochord—it may easily be demonstrated that (although the sudden closure of the same current produces a maximal twitch with subsequent persistent contraction) it now gives no indication of shortening, or, in the most favourable case, a weak persistent contraction only, in striated muscle. If the same experiment is repeated on a preparation of smooth muscle, *e.g.* the adductor of the shell in anodonta, the effect is quite different. Fick (4) indeed asserts that he has succeeded “in passing currents of considerable strength” through this muscle also, “without contracting it,” but a phenomenally slow increment of current intensity was required, extending over several minutes. Under these conditions it can hardly be a matter of surprise that no visible manifestations of excitation make their appearance, considering that the effect of the constantly increasing fatigue changes in the muscle-substance must be accentuated in proportion with the slowness of increase of intensity, at every point at which (as will be shown below) an excitatory process is discharged by, and during, the passage of the current. At each successive moment, *i.e.*, the current acts upon points of the fibre, which have already been modified by the whole preceding passage of current, in proportion with its duration.

Moreover, it is easy to show, as might be expected, that the molluscan muscle in its relaxed state is highly sensitive to the gradual entrance of current. If there is a rheochord in the circuit, with as many cells as would be sufficient to set up a strong closure contraction without the rheochord, an analogous change of form in the muscle, corresponding with the commencement of the persistent closure contraction, will invariably appear if the rheochord slider is gently pushed forward from the zero as evenly as possible. The contraction begins when the current has reached a certain intensity, the curve rising the more steeply in proportion with the rate at which the slider is pushed forward. We have thus found it possible to record marked effects when the intensity of current had been slowly increasing for two minutes; the experiment of course requires very sensitive preparations.

We may conclude from the preceding data that every change of form which can be termed a "twitch" in a suitable muscle, requires for its effective stimulus a more or less *rapid* positive or negative variation in current density, whether beginning at zero or at a finite value; and since, as at once appears when a muscle with parallel fibres is partially traversed by current (the case of total excitation will be treated later), each twitch corresponds with a wave of contraction spreading through the entire length of the muscle, the *transmission* of excitation from the seat of direct stimulation would seem in the last resort to be produced and conditioned by a rapid *variation* in the current. Hence, while strength of excitation depends fundamentally upon intensity, duration, and density of current, the discharge of a wave of contraction depends also upon the nature (steepness) of the increase of current intensity in the muscle.

These conclusions stand out more clearly from a simple, graphic representation (Fig. 81), after Fick (4, p. 28 f.) The abscissæ indicate the times, the ordinates correspond with the current intensity at the moment. While, in a given case, a passage of current, such as is represented in Fig 81 (a), may fail to excite both striated and smooth muscle, another process of current like Fig 81 (b) may be an effective stimulus for the latter. In order to produce the closure twitch in striated muscle a steeper rise in the curve of current density is essential. In variations of current, starting from and returning to zero, the following cases are conceivable: a variation of the form (Fig. 81, c, c),

corresponding with a single weak induction current, or "current-impact," does not eventually produce a twitch, as is the case in a variation of the form (*d*), because the low duration of current is compensated in the latter by greater intensity. On the other hand, a variation of the form (*e*) may act as a stimulus on the same preparation which is unexcited by (*c*), because in this case the greater duration compensates the lower intensity, and the same may also apply to a variation with less steepness of rise and fall (*f*).

The striking predominance of the excitatory effect of the

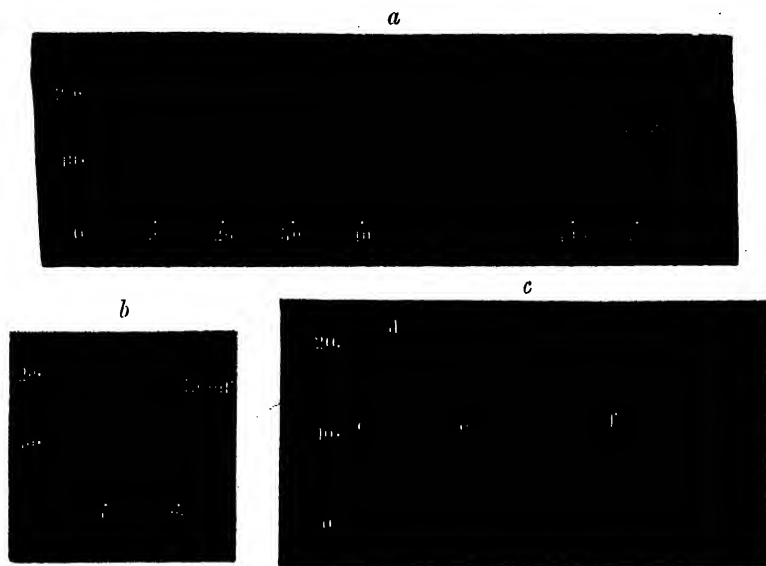


FIG. 81.—*a*, *b*, *c*, Different forms of variation curves of current intensity. (A. Fick.) The abscissae indicate the time in seconds, the ordinates the strength of current.

break induction current is usually referred to the different rise of current intensity, and applies as much to smooth as to striated muscle, and indeed to nearly all irritable tissues. But since the experiments in this direction have till now been confined almost entirely to motor nerves, it will be more convenient to postpone the discussion of these facts until the scanty experimental data which exist in regard to dependence of excitation on the exact *form* of the curve of variation of current intensity can be brought forward.

The reaction of cardiac muscle to the constant current, as in many other respects, is exceptional. Ever since Eckhardt

(11) observed the non-ganglionated apex of the frog's heart to pulse rhythmically, when a constant electrical current was led through it, this easily verified fact has been the subject of repeated experiments. The frequency of pulsation increases in a certain range with the strength of the current. We have already seen that cardiac muscle responds by rhythmical manifestations of excitation to other continuous, uninterrupted stimuli, *e.g.* mechanical and chemical, so that the effect of sustained passage of current as just described is nothing extraordinary, and the only question is whether this property really is specific to cardiac muscle, and is not rather a general characteristic, as it were abnormally developed. Hering (13) long ago observed that a curarised frog's sartorius became rhythmically excited under certain conditions when its intrinsic longitudinal current was short circuited by immersion in 0.6 % NaCl, and also when acted upon by very weak artificial currents, the reaction being similar to that of chemical excitation, according to Kühne and Biedermann. This however only referred to weak contractions in an unloaded muscle that was moreover dipping into fluid. Later on we succeeded in producing a long series of vigorous twitches, by means of uniform, persistent closure of a battery current, in a loaded sartorius extended in Hering's double myograph, provided the excitability of the muscle-substance was locally increased at the seat of direct excitation (*i.e.*, as will be shown, the cathodic end of the muscle) by treatment with adequate solutions of Na_2CO_3 , from 1-3 % (14).

Fig 82, *a*, shows such a series of curves, recorded after fifteen minutes' continuous action of a 2 % solution of Na_2CO_3 on the tibial end of a curarised sartorius, during closure of a medium descending current. A rapid shortening (twitch) of the muscle begins before the first pronounced twitch has expired, long before the descending shoulder of the curve has reached the abscissa. The superposition of three twitches in rapid succession brings the second contraction to the first maximum, after which follow in regular rhythm twenty-five vigorous single twitches, hardly inferior in size to the initial twitch; these, at first closely packed together, are discharged later at intervals of about one second. After the twentieth twitch, the magnitude of shortening diminishes rapidly, and at last only a trace of persistent contraction remains,

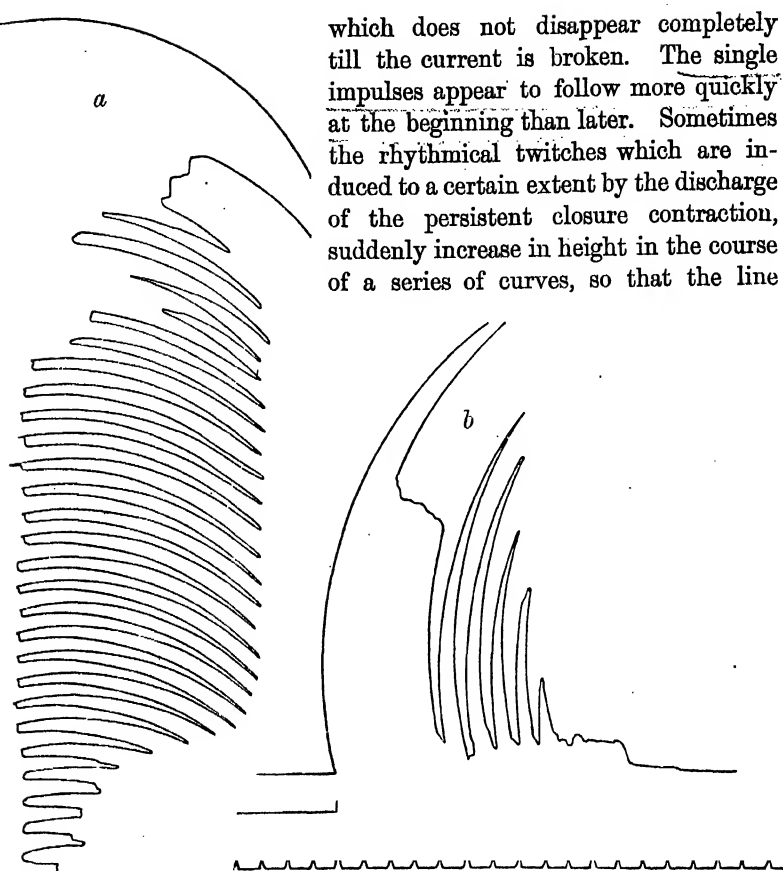


FIG. 82.—*a*, Two series of rhythmic twitches during persistent closure of a battery current (thermo-electric pillar, rheochord resistance 60), after fifteen minutes' continuous action of Na_2CO_3 (2 %) on the tibial end of the sartorius; *b*, second excitation of iscle, effect of fatigue.

which connects the summits at first rises steeply, and then sinks away again rapidly when the height of twitch decreases (Fig. 83)—a reaction which recalls the well-known staircase increment of twitch in different muscles, on exciting them with uniform induction currents.

Since on applying very strong currents—according to Hering very weak currents also—similar rhythmic manifestations of excitation, and but little less regular, may appear without any artificial increase of excitability, it is not unjustifiable

to assume that a sustained and persistently flowing current in many cases, perhaps always, sets up a discontinuous state of excitation, which only produces an apparently steady contraction, because the conditions of experiment are usually such that weak rhythmical contractions that are feeble in character or confined to single bundles of fibres, remain without visible, mechanical expression. From this point of view it would be legitimate to speak of tetanic closure twitches, and of a tetanic character of the persistent closure contraction; indeed it seems doubtful whether on exciting a curarised muscle with strong battery currents a simple non-tetanic closure twitch

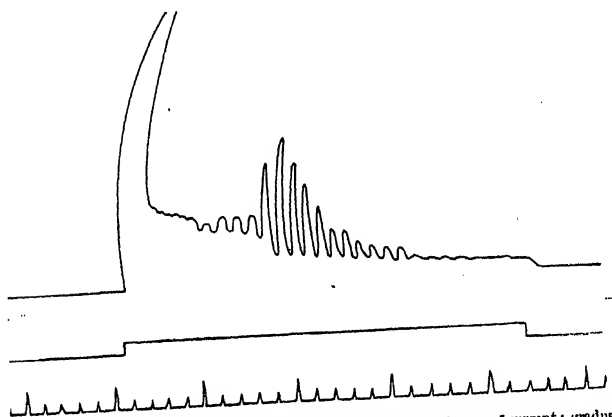


FIG. 83.—Rhythmical series of twitches from sartorius; persistent closure of current; gradual increment of twitches.

really can be obtained—the extended curve rather speaks in favour of this view than against it. How far it is really legitimate to draw inferences from this to the mode of action of weaker currents must provisionally be left undecided, just as it is not possible from our present experimental data to postulate the discontinuous nature of the persistent closure contraction, although there is much to be said for it. The constant current, during its closure in cardiac muscle, thus produces a regular and invariable series of rhythmical contractions, which also appear, at least under certain conditions, in striated skeletal muscle; and this is still more the case in smooth muscle. Engelmann (5) was the first to observe an appearance in the ureter of the rabbit, which may be regarded as the undoubted analogue of the facts under

discussion; *i.e.* the periodic waves of contraction that start from the kathode of the constant current, without any apparent shifting of the object upon the exciting electrodes. "The number of contractions observed during a closure of 1-2 minutes was less (2-3) with weak currents, and more (5-7) with stronger currents. The intervals at which the waves followed varied between 4 and 20 secs. The periods were frequently short and equal, in other cases they varied in duration. The ureter did not usually relax completely at the negative electrode in the interval between two waves—at least with the stronger currents (persistent closure contraction)." At break of the constant current again, Engelmann repeatedly saw periodic waves of contraction starting from the region of the positive pole in the rat's ureter (*l.c.* p. 414), a phenomenon to which we find an analogue in the fact, that the discharge of a persistent opening excitation in rhythmical single twitches may also be observed in the sartorius under the described conditions, though more rarely. As a rule, indeed, these are only more or less extended single twitches, and it is impossible to draw any conclusion as to their tetanic character.

No fundamental difference, therefore, obtains between the manifestations observed in cardiac, and in other, striated and smooth, muscle, during the constant passage of current; and it is only quantitatively that differences can be detected in the rhythmical discharge of excitation, which occurs invariably in the one case, and in the other only under certain conditions. The much slower succession of single waves of contraction in the electrical excitation of the ureter, is easily explained by the lower excitability and more sluggish reaction of smooth, as compared with striated, muscle. And (as we shall see below) a similar relation obtains between this last and the motor nerves, so that the same manifestation presents itself in gradations in the electrical excitation of smooth muscle, cardiac muscle, striated skeletal muscle, and motor nerves. Hence it can be seen that the succession of rhythmical excitatory impulses is generally more rapid in proportion as the excitability is greater. This appears not merely from the comparison of the effects of excitation in smooth and striated muscles, cardiac muscle and nerve, but also from the phenomena which may be observed at each single excitation of any one of these tissues. If, under the influence of current, or from any other cause, the excitability sinks

below a certain limit, the possibility of rhythmical sustained excitation disappears under all conditions; there can be nothing more than the discharge of a single twitch, or the development of a seemingly sustained constant contraction. We might attempt to find in these manifestations an exception to the statement that a "twitch" (or self-transmitting wave of contraction) is only excited by a more or less steep variation in intensity of the electrical current. But it must not be forgotten that this, in the last resort, signifies merely that the changes produced by current (as by any other mode of excitation) in the excitable substance must increase with a certain rapidity from zero, or from a finite value, if a wave of contraction is to be caused by them. More or less rapid variations of the state of excitability of an irritable substance are however conceivable, and really occur when the *cause of excitation* itself is constant; *e.g.* the pulsations of the apex of the heart in chemical or mechanical excitation. This obviously depends only upon the nature and state of excitability of the substance in question.

We have thus acquainted ourselves with the dependence of excitation on intensity of current, as well as on its duration and kind of increase in general; in conclusion we have to consider the effect of its direction. It is *a priori* evident that this can hardly play any part in the typical, longitudinal passage of current through a muscle with parallel fibres, if the muscle really is constructed with geometrical regularity, and, in particular, is of equal diameter at both ends, so that the density of the current at all points will be uniform. Such preparations, however, are rarely met with, and the generally adopted frog's sartorius (although comparatively regular) exhibits in this respect considerable variations. Before discussing this point in detail, we must consider the enormous influence exerted by the *angle of the current*, *i.e.* the angle between the lines of the current and the direction of the fibres.

The earlier observations on this point were very contradictory. Sachs (15) more especially maintained that muscle possesses equal excitability to transverse and to longitudinal passage of current, but the method which he employed leaves room for doubt whether an electrical current traversing the muscle in a really transverse direction can produce effective excitation. Two needles were used in these experiments as electrodes, and brought

into contact with the muscle in such a way that their line of connection cut transversely across the muscle-fibres, so that a current passing through the contacts must traverse the muscle *mainly* in a transverse direction. Yet it is almost self-evident that under these conditions, even with the most exact transverse passage, there must also be longitudinal lines of current. It would then depend merely upon the strength of stimulus whether these were able to provoke an excitation. Sachs contended that the strength of current, which is just effective in his experiments, acted through the lines of connection between the two electrodes only, but this, as was justly observed by Leicher (16), could only occur under certain non-existent premises.

A more satisfactory method, invented by Matteucci in 1838, and then applied to nerve by Luchsinger (17) at Hermann's instigation, consists in plunging the object to be traversed by the current (nerve or muscle) into an indifferent conducting fluid, which the exciting electrodes also dip into. In this case the muscle, which lies at right angles to the lines between the electrodes, is entirely, or at least mainly, traversed by vertical lines of current only—entirely when the electrodes are flat or linear, mainly when they are punctiform. Tschirjew (18), who used this method, found that greater intensity of current is required on exciting the muscle transversely than in longitudinal excitation, but he believed notwithstanding (taking into account Hermann's statement that the resistance of the muscle is much greater—4-9 times—in the transverse than in the longitudinal direction, so that a greater fraction of the current must pass through the muscle with longitudinal than with transverse stimulation), that muscle is more excitable to transverse than to longitudinal passage of current. Both this experiment, however, and those which Giuffrè, Albrecht, and Meyer (19) worked out under Hermann's direction, present weighty experimental objections, as Hermann himself pointed out. Tschirjew either placed the excised muscle in the excitation-trough, with silk thread attached to both ends, connecting them with a lever, or employed minute quadrants of muscle; while Giuffrè tried to avoid the difficulties due to irregularities of form in the ends of the muscle (*sartorius*) by dipping only the portion with parallel fibres, which he marked off with artificial transverse sections, into the fluid. Since, however, as will be shown,

the excitatory effect of a current is lessened to an extraordinary degree when it passes in and out by artificial sections, or otherwise injured points of the fibre, it is clear that in all these last experiments the relations of excitability may appear to alter in favour of transverse passage of current under certain conditions. And if a much lower excitability of muscle is really found to exist with transverse passage of current, it can only be

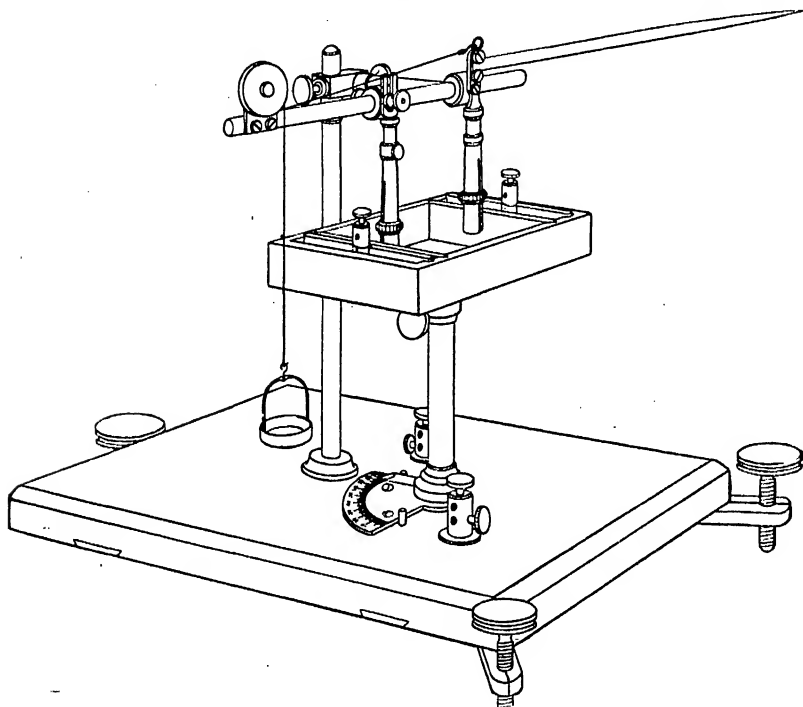


FIG. 84.—Apparatus for passing current transversely through the muscle (sartorius). (Hering.)
(Catalogue of Physiological Apparatus. R. Rothe, University Mechanician in Prague.)

viewed as an *a fortiori* proof that the latter is a weaker stimulus than the longitudinal current. The point has been experimentally decided by D. Leicher. He used apparatus, which corresponded essentially with the method employed much earlier by Hering for the same purpose (Fig. 84). The muscle (curarised sartorius) was fixed between two clamps by the bones at either end, just as in Hering's double myograph. One clamp is fixed, the other is left free, and communicates the movement of the

muscle to a lever. The excitation-trough consists of a parallel-epipedic ebonite box, the shorter walls of which are lined with amalgamated zinc plates, which lead in the current. At some distance from these are two other walls of baked porous clay, so that a canal is formed on each side, bordering on the somewhat quadratic inner space of the trough. This contains 0.6 % NaCl solution, while the two canals are filled with concentrated solution of zinc sulphate. The muscle, conveniently stretched by a weight, and quite uninjured, is plunged into the centre space, so that the angle formed by the current in its passage can obviously be altered in any direction by simply turning the trough round.

As might be expected with true longitudinal passage of current (angle 0), the make twitch, or persistent make contraction, appeared, just as outside the fluid, but Leicher never observed an effective opening excitation with the strength of current employed (9 Dan.) If a current traverses the muscle at an angle of 45° , it still has a certain effect, but much less than with true longitudinal passage. "Finally, if the muscle is traversed at an angle of exactly 90° , it usually remains quiescent. More rarely with transverse passage a weak excitation occurs, which, notwithstanding its inferior magnitude, varies in response to any alteration of current." *The total non-excitability of striated muscle to electrical currents perpendicular to the fibre-axis* must after these simple demonstrations be accepted as proven. It is easy to understand that the experiments in a typical form could only be carried out on a muscle with parallel fibres constructed as regularly as possible, and that any preparation with a more complicated arrangement of fibres is *a priori* excluded. There are no corresponding experiments on smooth muscular parts, but it may be assumed that here also, in so far as the contractile fibrils run parallel, they give no response to the transverse passage of current. It is clear that the fact of the dependence of excitation upon the magnitude of the angle at which the contractile parts, lying in a definite direction, are traversed by the lines of current, is of the greatest significance to the theory of the action of the electrical current. Before entering upon this in detail another fundamental law of electrical excitation must be considered, in regard to the question *at what point of the tract in the muscle directly traversed an*

excitatory process is set up by the current at its commencement or end, as well as during its passage. The immediate presumption which, at least for induced currents, was for long the only accepted theory, is obviously that excitation occurs uniformly at every point of the area traversed, so that when current passes through the muscle longitudinally, each transverse section falls into simultaneous, and, in so far as the excitability everywhere is equal, uniformly strong contraction. The bare consideration of a striated muscle stimulated by closure or opening of a current gives no certain conclusion, for there is always, even in such cases, an apparently simultaneous shortening of the *entire* muscle, which must be due to an undulatory progress of the contraction, as, *e.g.*, in the partial excitation of a muscle with parallel fibres. The question must either be decided by delicate methods of time-measurement, as in the determination of rate of conductivity, or by experiments on muscles in which, as in smooth fibre-cells, the processes of contraction and conduction are uniformly slower. Both lead to the same end eventually. If total longitudinal passage of current in a parallel-fibred, cross-striated muscle, *e.g.* sartorius, produces excitation which is transmitted in undulations from one pole to the other, it must obviously be possible, by means of two levers that rise successively at different points of the muscle, in consequence of the wave of contraction which passes under them, to obtain two curves of expansion, which, when the lever points lie vertically one over the other, must easily show whether the two levers rise simultaneously or no; in the second alternative, the localisation of the difference enables us to see in which direction the wave was travelling. Aeby (20) tried to decide the question experimentally on this principle. He laid two levers on the curve of the horizontally situated curarised muscle, at a distance of 17 mm., which recorded the expansion of the muscle, in consequence of functional activity, on a rapidly rotating cylinder, and found that both levers were *simultaneously* raised from the muscle when it was excited by the make or break of a constant current passing through it. This would to all appearance have been impossible if excitation had really started from one end of the muscle only. The result of this experiment is therefore in direct contradiction with the preceding theory of a *polar* excitation of the muscle.

Von Bezold (10) tried to solve the problem by a different

method from that of Aeby. He employed the ordinary myograph, in which the longitudinal alteration of a muscle or fragment of muscle is recorded, using the latent period of the make and break twitch as his criterion. The curarised sartorius was fixed by its upper end to a cork trough fitted to its size, so that two copper wires crossing the muscle at right angles to the direction of its fibres clamped a certain portion of its length, about 4 mm., between them, to two points in this trough. The ends of these two wires served to fix the muscle to the cork, and made the electrodes. The portion of muscle between them was thus at the same time the tract traversed by the current. If the current entered the muscle by the lower electrode, nearest to the recording end, *i.e.* was, as v. Bezold expresses it, an ascending current, the resulting curve showed that a longer time elapsed between the moment of closure and the beginning of the twitch than when the current left the muscle by the lower electrode, *i.e.* was descending. In the first case, according to Bezold, the excitatory wave arising at the upper (negative) electrode, had to spread itself over the intrapolar tract, which was fixed at both sides, before it could enter the free portion of the muscle below and through the lower (positive) electrode; in other cases the excitation started from the lower electrode (which was now negative), and passed immediately over to the free part of the muscle. The difference in the two times which elapse between the moment of closing the current and the beginning of the twitch corresponded to the time required by the excitation to traverse the intrapolar tract of 4 mm. Von Bezold showed by the same method that on opening the circuit the excitation started at the positive electrode. Aeby disputed the conclusions of v. Bezold's experiments, but as Hering remarks (*l.c.* p. 248), it is impossible to account for the time differences found by v. Bezold, and constantly recurring in the same sense, in any other way than by the different *direction* of the current. The marked variation in magnitude of time-difference, amounting to between 0.005 and 0.025 (average 0.012) secs., is perhaps, according to Hering, to be explained by the fact that the conductivity of the muscle is disturbed in a different degree at the part clamped, according to the amount of pressure put upon it. Taking for granted then that the time from the moment of closure or opening to the beginning of the contraction is really longer when the upper contact makes the

kathode at closure and the anode at opening, it may further be asked how far the different direction of current accounts for this disparity. This question, however, is answered by v. Bezold's hypothesis, according to which the direct conclusion from the above experiment is as follows: "*That on the closure of a constant current, (striated) muscle is at first excited in the region of the negative electrode and not in the region of the positive electrode, while on opening the current flowing through the muscle, the immediate excitation would be at the positive and not at the negative pole.*"

These data of v. Bezold, and the conclusions drawn from them, are borne out by the well-known fact that, on exciting with the constant current under certain conditions (*i.e.* diminished conductivity), the manifestations of contraction are confined to the region of the point at which the current leaves the muscle (kathode), and that this occurs invariably in the persistent closure contraction when currents that are not unduly strong are sent into the muscle. With reference to the first point, v. Bezold refers back to an older observation of Schiff (21), who found that when a moribund muscle had already ceased to yield a closure twitch there was still at the negative pole of a constant current a weak, localised idio-muscular contraction, far less distinctly expressed than the effect of mechanical excitation, which persists uniformly so long as the current continues, and then dies away again. It is not difficult to show that this "idio-muscular" kathodic persistent contraction is completely identical with the persistent closure contraction described above, provided the currents used for excitation are not excessively strong. Engelmann (5) obtained direct experimental proof that in perfectly fresh muscle also the sustained contraction following on the closure twitch is confined to the region of the kathode. The method of his experiment is evident from the accompanying diagram (Fig. 85). Engelmann passed a current through the entire sartorius, and fixed the upper section with a clamp which was 7 mm. or more below the upper electrode, while the lower electrode was formed by a wire hook introduced into the muscle. The section of muscle below the clamp was therefore the only movable part, and recorded its contractions upon a slowly travelling surface. When the current in the muscle was descending, the lever remained above the abscissa after the make

twitch had expired, as long as the closure lasted; when, on the other hand, it was ascending the lever returned to the abscissa completely after this twitch. By the same method of experiment, moreover, it is easy to establish v. Bezold's conclusions. In two experiments Engelmann found that the closure twitch began 0.006 secs. and 0.009 secs. later with an ascending than with a descending current, which must be explained by saying that in the ascending current the contraction discharged at the upper end of the muscle must first be transmitted through a tract of muscle 7 mm. long before it can act upon the lower movable section of the muscle. The localisation of the closing, as well as opening, persistent contraction, is elegantly shown by the

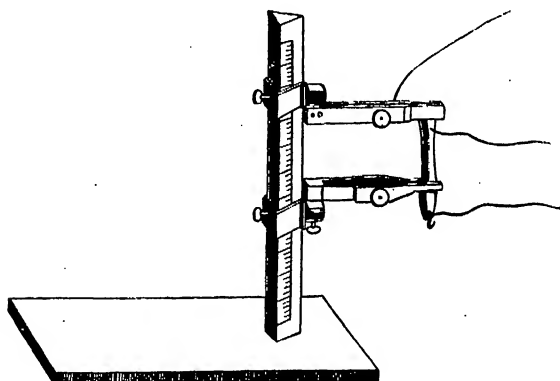


FIG. 85.

following method, taken from Engelmann. The curarised sartorius is extended in Hering's double myograph, with non-polarisable electrodes, which in this case are *both* free. In order to observe the changes of form independently in either half of the muscle, its centre is fixed by a clamp specially constructed for the purpose. This consists of two troughs, not exceeding 5 mm. in length, supported by a pillar, and covered with a layer of oil clay (Fig. 71). The clay moulds itself firmly to the shape of the muscle, holding it sufficiently by contact alone, with no perceptible pressure, to prevent a direct transfer of the changes of form from one half of the muscle to the other, without inhibiting the transmission of the excitatory process. The non-polarisable electrodes make it possible to continue the passage

of current through the muscle as long as is required, without any fear of the intensity of the current diminishing in a perceptible degree; and this is facilitated by the study of the persistent opening contraction. It is at once seen that first one and then the other half of the muscle, according to the direction of the current flowing through it, becomes permanently shortened (Fig. 88), and that on strengthening the current the persistent contraction increases considerably (Fig. 78), without any transfer to the other (anodic) half. If a muscle that is not too tensely stretched is examined with the unaided eye or magnifying lens, the local swelling of the ends of the fibres may be plainly seen, even with minimal currents, after the closure twitch has expired, as described by Engelmann. The contractile substance almost appears to flow suddenly, as it were, at the moment of closure, from the region round the kathode to the kathode itself, and to accumulate there. In muscles that have been exposed to excess of cooling, by which their conductivity has suffered, it can be seen directly, as shown by Hermann, that the muscle is drawn at closure towards the kathode, on opening towards the anode. The swelling only affects the peripheral ends of the fibres, immediately before they pass into the tendon. Even with moderately great tension of the muscle, a small swollen expansion appears, which persists unchanged throughout the entire duration of a persistent passage of current. On strengthening the excitatory current the persistent closure contraction increases considerably in amplitude, without however losing its localised character, even with high intensity of current. The sections which lie collectively between the kathode and the centre of the muscle never remain in persistent contraction during the passage of current. In judging of the spatial extension of a manifestation of contraction in muscle, great care must be taken not to confound the true shortening with the merely passive contraction of adjacent parts. A very simple method of artificial observation consists in marking the surface of the muscle with signs, which move in opposite directions when the muscle shortens, and thus indicate the spatial extension of the contraction. We have found it convenient to paint the whole muscle with transverse bands of Indian ink, at right angles to the direction of the fibres, so that the distance between each pair of cross-lines, traced with a fine bristle upon the dry surface of the sartorius, was about $\frac{1}{2}$ mm.

Each contraction, however small, was then defined by a more or less considerable reduction in one or more of the cross-bands or the coloured spaces between them. Within the passively participating muscle tracts, on the other hand, the coloured cross-bands are much contorted, but do not appear to get smaller. In very widely extended tracts they grow considerably broader, as will appear below (22).

In a tracing—conformably with direct observation—the persistent closure contraction only appears in the curve corresponding with the kathodic half of the muscle, but if the currents employed are not too strong (Figs. 77 and 78) the closure twitch is seen on both sides equally. It is only with the weakest minimal currents that the twitch appears higher on the kathodic than on the anodic side, where it is sometimes no more than a little hump. This marked difference, which is plain with the application of the weakest currents, occasionally persists for a considerable period, disappearing, however, as a rule (provided the excitability and conductivity of the muscle have not otherwise suffered), at an intensity of current which may still be termed low, giving place to complete uniformity of twitch on either half of the muscle. The assumption that the mechanical conditions of shortening are less favourable in the one half than in the other is easily shown by control experiments to be inadequate, so that the behaviour of the sartorius towards the weakest minimal closure stimuli, as described, is no less calculated to confirm v. Bezold's theory of the seat of direct excitation by the current, than, with application of stronger currents, the fact of localisation of the persistent closure contraction. These experiments show further that the waves of excitation, *i.e.* contraction, may die out on passage through the intrapolar tract if the discharging stimulus is very weak, and that with somewhat stronger stimuli they are propagated in a diminishing degree (with a decrement) in the anodic—or, at the opening excitation, kathodic—half of the muscle. This is quite evident in a prolonged series of twitches obtained by repeated closure at uniform strength and direction of current. Here the height of the curve of the twitches decreases more rapidly than the magnitude of the sustained contraction, which still appears at each new closure, even when the make twitch has completely died out on the kathodic side. On the other hand, the unequal decrease in the height of the closure twitch on the kathodic and anodic

sides respectively is very apparent during the process of "fatigue"; both curves are almost equal in height at the beginning. The anodic twitch is later only half as high as on the kathodic side, and finally disappears altogether, while the latter is still twitching visibly (Fig. 77). If the intensity of current exceeds a certain limit there is regularly an apparent invasion of the persistent closure contraction, which starts at first from the kathodic end only, and spreads over the fixed centre of the muscle. This phenomenon is most conspicuous with currents that are inadequate to produce an effective break excitation at the usual period of closure. It is very remarkable that the degree of persistent shortening, is not, as might *a priori* be expected, under all conditions higher on the kathodic side than on that of the anode, but *with currents of a certain strength the ratio is usually augmented*. Aeby (20) drew attention to an analogous relation for the closure twitch, when he found that the ratio of height of twitch in either half of the muscle was inverted with stronger currents, and under the influence of progressive fatigue—the twitches of the anodic half, which at the beginning were equal with or smaller than those of the kathodic half, gradually becoming larger than the latter. Indeed it may happen that—conversely to the case of currents of medium intensity—the kathodic half will exhibit only a weak sustained contraction, while the anodic half still twitches plainly at each new closure.

The asymmetry of the sartorius is very disturbing in all these experiments, since, as we shall see, it produces an *a priori* inequality of excitation effects in the two halves of the muscle with alternating direction of currents. This agrees with the fact that the diffusion of the persistent closure contraction over both halves of the muscle already referred to always shows itself earlier, and is much more marked, with an ascending direction of current (*i.e.* from knee end to pelvic end), than with a descending current. This is the more remarkable since, in consequence of the increasing density at the small, tapering, lower end of the muscle, and the more pronounced make excitation produced by it with a descending direction of current, the opposite might rather have been expected—if with increase of current the magnitude of the make twitch and the degree of diffusion of the persistent closure contraction really depend essentially upon the strength of excitation *at the kathode*.

But, as we shall see later, the sustained contraction appearing under these conditions in the anodic half of the muscle is really a manifestation *sui generis*, and does not stand in any causative connection with the normal persistent kathodic closure contraction at the ends of fibres. With regard to the *localisation of the break excitation*, we must further remark that it takes effect at the anode in exactly the same way as the *make excitation* at the kathode, since at first only the corresponding half of the muscle twitches, and it is only later, when the excitation at the anode has reached a certain magnitude, that the wave of contraction propagates itself through the entire muscle, and this with a perceptible decrement, expressed in the different height of twitch in either half. The *persistent opening contraction* is similarly localised in the region surrounding the point where the current enters.

With the exception of the persistent closure contraction on the side of the anode, occurring as described under certain conditions only, it cannot be denied that the facts above stated are collectively much in favour of v. Bezold's view of a *polar* excitation of muscle by the current. Notwithstanding this, however, the localisation of the closing and opening persistent contraction cannot be taken *per se* as a strong proof of its validity. For if the persistent closure contraction seems to be localised in the region round the point of exit of the current, the objection may be, and actually has been, made (Brücke, 23), that the current has an excitatory action upon the whole tract, taking further into consideration that this direct excitation in the region of the anode soon becomes ineffective in consequence of a depression of excitability proceeding from the same region. Against this, again, there is the extraordinarily limited diffusion of the persistent kathodic closure contraction, as is readily ascertained from mere inspection. It appears desirable to collect more evidence, and in particular to determine positively the fact that at each closing twitch a wave of contraction proceeds from the kathode, at each opening twitch from the anode. Here, again, the method of clamping the muscle by its centre, as described above, affords excellent experimental possibilities.

Before entering more minutely into the question it will be as well to determine the fundamental point of *what is to be understood in the electrical excitation of a muscle by kathode and anode*.

In the majority of the older experiments, where the current was led in through metal wires, in direct contact with the muscle, there can, of course, be no doubt as to the meaning of the terms anode and kathode. So, too, in v. Bezold's experiments, the expression "the closing excitation proceeds from the kathode, the opening excitation from the anode," cannot well be misunderstood. But the case is otherwise when, although metal conductors are used, the current is led into the muscle *via* bones and tendons. Then the expression quoted takes on quite another meaning. It is obvious that the excitation cannot proceed in this case from those points at which the metallic electrodes are in contact with animal tissues, *e.g.* the bones or tendons; but that the tendinous ends of the muscle-fibres themselves are the *real* electrodes, and when, under these circumstances, electrodes are spoken of, it can only mean that the current sets up a peculiar action at the *points at which it enters or leaves the muscle-fibres*. How easily misunderstandings may arise through these ambiguities, is evident from the consideration of certain experiments of Aebj (20) and Brücke (23), which are intended to disprove v. Bezold's theory. The former sent current through both legs of a frog still united by the pelvis, so arranged that the wires which served as electrodes were connected with the lower ends of the two legs. A piece of the thigh-bone was cut out on either side subcutaneously, so that the muscles of both thighs shortened at closure of the current, but more so with a descending than with an ascending current. Aebj deduced from this that the former lay nearer to the negative—as he thought, more active—pole; thereby, as Engelmann pointed out, confusing the real, or natural, electrodes of the muscle with the artificial—*i.e.* unreal—electrodes of the entire preparation. For obviously, in a thigh traversed by an ascending current, the anode would occur at the knee, the kathode at the pelvis, and *vice versa* in opposite cases. Brücke used a similar preparation, only he removed the entire skin, with the extensor muscles, together with the diaphyses of the thigh-bones. If he gripped the two gastrocnemii with forceps, connected in circuit with 6–10 small Daniell cells, the muscles of the thigh and leg contracted on both sides. "In this case," says Brücke, "no contraction waves could spread from the kathode to the flexors of the thigh. It must be admitted that they contracted independently of all kathodic action, solely because they were traversed by

the current ; otherwise it must be assumed that the knee-joint on the kathodic side, or the remains of the pelvis on the anodic, act as kathode for the thigh muscles." But as Hering showed, this view is that which was long ago opposed by Engelmann, since for him the anode is the place where current enters the muscle-fibres, the kathode the place at which it leaves them. Hering (*l.c.* p. 241) expresses this more exactly as follows : *the real physiological anode in the muscle is formed by the collective points at which current enters the contractile substance ; the physiological kathode by the collective points at which it leaves them.*

This proposition leads to a corollary, best expressed in Hering's own words. "If we picture the entire current which traverses the muscle longitudinally to be divided into single lines of current, these would indeed, generally speaking, lie parallel with the direction and limits of the single fibres in a parallel-fibred muscle, and the collective anodic points would lie at one end, the collective kathodic points at the other, of the muscle ; in detail, however, there would be innumerable exceptions. In the first place, quite apart from any tendinous intersections, we must consider the case in which the single muscle-fibres end at different points of the muscle, although the bulk of them may be approximately as long as the muscle itself. But directly such muscle-fibres occur, the points at which the current enters or leaves are no longer to be sought exclusively at the ends of the muscle, and besides the chief centres of polar current action, other centres will be distributed in the muscle.

"Moreover an absolute parallelism between the lines of current and the muscle-fibres cannot, as a rule, be predicated, particularly where the muscle is not extended, or is subjected to pressure at any spot, or if its surface is not entirely freed from the remains of adherent conducting matters, solid or fluid.

"In muscles which are lying relaxed upon a slide, the fibres, as we know, by no means invariably run straight, but are often undulatory, especially after a preceding twitch of the muscle, because they cannot elongate again on account of the friction on their under-surface. A current traversing the muscle longitudinally would then find innumerable points of entry and exit along the edges of each individual muscle-fibre, and it would be quite fallacious to place the physiological anode and kathode exclusively at the ends of the muscle. If the muscle is clamped

at any point of its course, considerable bending of part of the muscle-fibres is inevitable, especially if the muscle is pressed between two forks, with converse surfaces. The same thing occurs when a lever or button is placed on the muscle, and presses on it at the points of contact. In all these cases, part of the current must pass in and out of the contractile substance in a number of muscle-fibres at the seat of pressure."

These observations will show why the negative results of Aeby's experiments (*supra*)—in which, when a parallel-fibred muscle is wholly traversed by current, the propagation of a contraction wave is demonstrated by a lever—cannot be regarded as conclusive against the positive results of v. Bezold. In Aeby's experiments, a very considerable bending of fibres occurs at both points at which the lever is laid upon the muscle. Aeby himself remarks that "the lever was pressing somewhat upon the surface of the muscle." So that the current at the point at which the fibres bend inwards may very well pass in and out at different points of the contractile substance, and thus produce a direct excitation.

Under these conditions, new experiments *re* the polar effects of the electrical current appeared desirable. The clamp experiment (Engelmann) with the frog's sartorius, as described above, in which the excitation passes the fixed point without difficulty, while the direct transmission of contraction from one half of the muscle to the other is made quite impossible, affords a simple method of graphically recording the course of the contraction wave, and so making measurement possible; for if excitation starts from the kathode on closure of the current, a muscle, fixed in this manner, and traversed by current in its entire length, must twitch in the half corresponding with the kathode earlier than the anodic half. The latter only begins to shorten when the wave of contraction proceeding from the kathode has passed beyond the clamped part. The time difference at the beginning of the contraction of the two halves obviously corresponds with the rate of transmission of the excitation, *i.e.* contraction wave, from the kathodic end to the first section beyond the clamp.

The method of experiment was as follows: a tuning-fork, making 353 vibrations per sec., and provided with a lever, served as the time-marker. This, together with a double myograph,

with non-polarisable, movable electrodes, stood in front of a vertical cylinder, which turned upon a crank, and the contractions of both halves of the muscle were recorded on its smoked surface, so that the point of the tuning-fork lever lay vertical to the two muscle levers, which move (up and down) in opposite directions; in this way it is possible, independent of the rate at which the cylinder rotates, to measure the difference in time between the beginning of the two twitches as well as the period of latent excitation, if the experiment is arranged so that the tuning-fork begins to vibrate at the precise moment of closure or opening of the current, as may easily be effected by withdrawing a conducting wedge introduced between the limbs of the fork (Fig. 86).

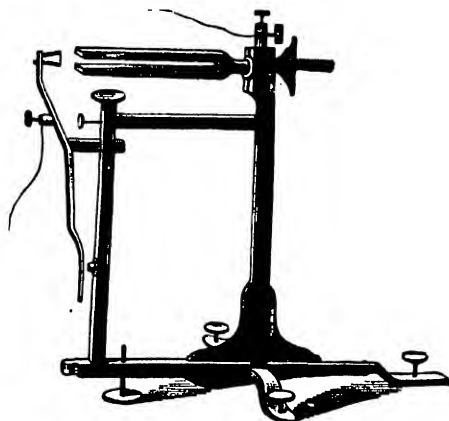


FIG. 86.—Registering tuning-fork, for interruption or closure of current. (Hering.)

By this method two curves of twitch are obtained with the closure of a battery current of sufficient intensity, one traced upwards and the other downwards, which are always in such relations with each other that the curve corresponding with the cathodic half of the muscle rises perceptibly earlier from

the abscissa than the other (Fig. 87, *a*, *b*).

If a perpendicular is drawn from each abscissa at the point at which the curve commences, the number of tuning-fork vibrations enclosed between the two perpendiculars gives the rapidity at which the wave of contraction, measured from its point of origin at the kathode to the first muscle section beyond the fixed spot, is transmitted. The length of this tract is 20–27 mm. according to the size of the frog; this corresponds with 4–6 vibrations of the tuning-fork, and the velocity of the make excitation is therefore 1–2 m. per sec.

The same method may be employed to investigate the time-relations of the break excitation. Since the denervated muscle reacts more slowly to the break stimulus, the intensity of

current must be considerably higher. Moreover, as we have seen, the *duration* of current is of great moment; at break excitation, the anodic half of the muscle invariably begins to twitch before the kathodic half, and the two curves seem in this way to be relatively altered (24).

Constant currents of very short duration (current impacts) and single induction shocks are, as a rule, effective only at their commencement, and not at the termination of the current. Chauveau observed in the muscles of living, warm-blooded animals, that weak induction currents, and currents from a Leyden jar, excite primarily in the kathodic region, and Engelmann emphasises the entire correspondence of action between short battery currents and single induction shocks, showing that an induction shock sent through a long strip of rabbit's ureter at most discharges a wave of contraction at the seat of the kathode, while it is only with very great excitability, and currents of marked intensity, that contraction sometimes appears to begin simultaneously at both poles. It is not difficult to demonstrate the same effect in striated muscle with similar excitation. If the curarised frog's sartorius is again experimented on, and excited by a fresh induction shock, the curve of twitch corresponding with the kathodic half will always, after a brief latent period, rise earlier from the abscissa, than that corresponding with the anodic half, in the muscle stretched in the double myograph, and clamped in the middle.

With higher intensity of induction currents, however, the anodic break stimulus also seems to become effective, which is not surprising after Engelmann's experiments on the ureter. Regeczy (25) fixed the sartorius like Engelmann by clamping it in the centre more or less firmly with ivory forceps, the other end being immovably fixed by another forceps; the lower end was connected with the lever of the myograph. The lower electrode was connected with the forceps fixed to the centre of the muscle, the upper one was attached to the upper end of the muscle (cf. Fig. 85). The direction of the induction current (coil at maximum strength) can be changed by a reverser. No difference was found in the size of the latent period with ascending or descending currents, as might have been expected from the experiments of v. Bezold, Engelmann, and Biedermann, with battery currents. While with weak induction currents the excitation starts from the kathode

only, the possibility of *bipolar* excitation with stronger induction currents is indicated by these experiments. The excitation at the kathode must, of course, be regarded as a closing, that at the anode as an opening, excitation.

We have already seen that the direction of current, with true longitudinal passage through a muscle with parallel fibres, would theoretically have no effect upon the consequences of stimulation, but that the sartorius in this very respect gives a varying reaction, owing, no doubt, fundamentally to its asymmetrical structure, and the consequent difference in current density at either end. On careful gradation of current intensity with the rheochord, it may be seen in every case that the closure of the descending current regularly produces the first excitation in the longitudinally traversed sartorius; it is only with greater intensity of current that the closure of the ascending current also becomes effective; a more or less evident difference in favour of the downward direction of current is still noticeable in many cases. As a rule, however, this difference, which is at first conspicuous, grows less and less, until at last with stronger currents it becomes imperceptible. The opposite effect occurs with the break excitation, to which the ascending direction of current is favourable. The point of the greatest density of current is found on sending current longitudinally through the sartorius at the lower end of the muscle, and corresponds with descending direction of current to the point at which it leaves, with ascending current to the point at which it enters, the muscle-substance. Since in the former case the closure twitch, in others the opening twitch, appear earliest, these facts alone show the probability—though only for currents of not too great intensity—that *the closing excitation proceeds from the kathode, the opening excitation from the anode* (24).

Again, with respect to the duration of the latent period, the difference in density at the two ends of the longitudinally traversed sartorius is very conspicuous. This is as true of the make as of the break excitation, the latent period being in fact invariably shorter when the excitation starts at the lower (knee) end of the muscle, provided the strength of current in both cases is uniform (Fig. 87, *a*, *b*). Tigerstedt subsequently obtained the same results (2, p. 185 ff.)

In view of the fundamental importance of the law of polar

excitation, it is desirable to bring forward as much, and as well-substantiated, experimental evidence as possible in its favour. Although the results already quoted might seem to be sufficient proof, the reaction of partially injured muscle to the passage of an electrical current is of special interest, since it not only affords a direct proof of polar excitation in v. Bezold's sense, but is also of great moment in the theoretical action of the current.

If the sartorius of a deeply-curarised frog is exposed as care-

a



FIG. 87.—a, Closure contraction, ascending direction of current (the kathode lies at the pelvic end of the sartorius). The lower line corresponds with the cathodic half. b, Closure contraction, descending current. The upper line corresponds with the cathodic half of the muscle.

fully as possible, and stretched in Hering's double myograph, the make excitation—which previously appeared in approximately equal proportions with either direction of current—will, when one end of the muscle is crushed by forceps, be altogether abolished or considerably weakened, while the effect of the closing excitation, if current is reversed so that the kathode falls on the uninjured end of the muscle, remains unaltered. The break excitation seldom comes about even after long-protracted passage of current, if the anode is on the injured side (26) (Fig. 88).

The effect of partial destruction *by heat* is much more pronounced than that of mechanical injury, since after the application of a "thermic transverse section" the excitability of the muscle to currents of medium intensity is in every case entirely, or almost entirely, abolished, when the effective electrode happens to be at the end that is in heat-rigor. Since both mechanical injury and thermic destruction produce a swelling of the end of the muscle, as well as other disturbances of the regular processes of the fibres, it is desirable to employ a method which

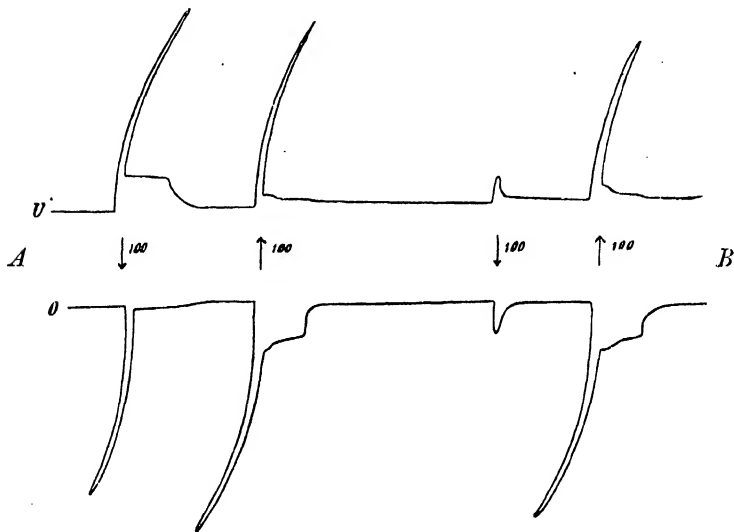


FIG. 88.—Twitch curve of sartorius fixed in the middle and stretched in the double myograph. (U=under, O=upper half of the muscle.) Effect of injury (death) of one (the lower) end of the muscle. The pair of twitches, A, were recorded before, B, after injury.

will kill the muscle, while avoiding these injuries as far as possible. Such is local freezing, according to Kühne's method, in which the form of the muscle-end scarcely alters perceptibly. If, in addition to this, the muscle is immersed in some indifferent fluid traversed by parallel lines of current, the methods of Engelmann (22) and Bernstein (16) will be still more exactly carried out in this experiment, since the effect of the asymmetrical form of the muscle is here totally excluded.

The preceding experiments of time measurement prove that induced currents have the same effect upon striated muscles as constant currents of very short duration, and accordingly that

the process of excitation is, as a rule, discharged only at the kathode. If it is further remembered that the break shock excites less strongly than the make shock, it is easy to comprehend the sequence of phenomena which are observed when a curarised sartorius is stimulated with gradually-increasing make and break shocks, sent in throughout the length of the muscle.

It was shown above that the difference in current density, due to the form of the muscle, at the points at which the current leaves and enters, occasions the dissimilar effects of excitation in the descending and ascending constant currents: this is equally the case with the induced current, so that the polar action of the latter may be taken as proven. The experiment is even more convincing with muscles that have been injured at one end. Both make and break induction currents, sufficient in intensity to produce maximal excitation in the uninjured sartorius, when the kathode lies at the end nearest the tibia, first produce excitation after mechanical, thermic, or chemical destruction of the latter, when the intensity of current has been strengthened by pushing the coil up considerably further (26). If the injury of a muscle with parallel fibres is not confined to one end, but both are destroyed, excitation fails with both ascending and descending direction of current, so that a muscle-fibre bounded by two artificial cross-sections, traversed in its total extension by parallel lines of current of equal density, remains unexcited whether the current axis is parallel with, or at right angles to, the axis of the fibres. Under certain conditions, when there is any opportunity for the arising of effective longitudinal components, excitation will occur sooner than it does with pure longitudinal currents. With the aid of the method of sending current transversely through the muscle described above, these facts may easily be verified, and serve to explain the frequent statement that the transverse excitability of muscle is less than its longitudinal excitability. This applies in particular to Giuffrè's experiments, in which bits of muscle were employed bounded on both sides by an artificial cross-section.

In interpreting the peculiar effect exerted by local injury (death) of the ends of the fibres upon the excitability of the muscle, with longitudinal passage of current, it is very significant that total death of the fibre-ends is not essential, certain *chemical* changes of the muscle-substance being all

that is required to produce these conspicuous manifestations of electrical excitation. Most of the salts of potassium are known to be acute muscle poisons, since when introduced in bulk into the circulation, or applied locally, they exercise a highly depressant, or inhibitory, action upon the excitability of striated skeletal and cardiac muscle; many acids are hardly less inimical to muscle-substance, even when highly diluted. It is easy to demonstrate that local treatment of one or the other end of the sartorius with these substances, which are inimical to excitability at the point of application, produces a reaction of the muscle to current analogous to that with localised death of the fibres. The method of experiment is the same as above. The chemical substances to be investigated are diluted in various degrees by moistening the thin (knee) end of the sartorius with a pad of cotton-wool soaked in the fluid required, or by dipping the vertically dependent muscle into it. The effects are most striking with the application of highly dilute (1-2 %) solutions of acid potassium phosphate, or a solution of meat-juice saturated with the same. After five to ten minutes' persistent action on the tibial end of the muscle, the excitability to closure of the descending, and opening of the ascending, current is invariably more or less diminished, so that the manifestations of contraction fail altogether, or are conspicuously lessened, if the effective electrode is situated at the end of the muscle that is undergoing chemical alteration (26). It must be remarked that here, as in the previous experiments, it is not complete *abolition*, but only *diminution*, of excitability to one direction of the current, caused by local "fatigue," that ensues, so that strong descending currents will still excite a sartorius treated as above, although no perceptible movement of the muscle responds to the impact of a weaker descending current, even when its intensity is quite adequate to produce a maximal closure excitation in an ascending direction.

From these results we must conclude that *in all the above cases it depends not so much upon the actual death of the contractile substance in any localised spot, as upon the consequences of chemical alteration in the same, whether, and to what degree, the closing and opening excitation become effective at the point of stimulation; and this is forced upon us still more by the fact that with local application of dilute solutions of salts of potassium, the normal*

excitability to both directions of current is completely recovered after washing with 0.6 % NaCl solution in a short time (10–15 minutes). It need hardly be said that this is as impossible after the application of substances which produce deep-seated chemical and physical changes in the contractile substances, *e.g.* sublimates, strong acids, alcohol, etc., as after mechanical or thermic destruction (26).

The corresponding sodium salts, which are in such close chemical relation with the salts of potash, exhibit a striking antagonism in their physiological effect upon striated muscle. We have already seen that the excitability of certain contractile substances (spermatic filaments, ciliated cells) is considerably heightened by Na_2CO_3 in dilute solutions, and in discussing the possibility of rhythmical excitation of striated muscle by the constant current it was pointed out that the effect was accentuated in a marked degree when the excitability of the *kathodic* end of the muscle was increased by treatment with Na_2CO_3 . If the pelvic end of an uninjured curarised sartorius dips into a 0.5–1 % solution of this salt, the excitability of the muscle to the closure of weak ascending currents is seen after a short time to be extraordinarily augmented, while the descending current still works quite normally, although break excitations are discharged with such low intensity of current and brief duration of closure, as would not occur in a normal muscle (26) (Fig. 89).

Sometimes under these circumstances, with weak descending currents, the opening twitch is conspicuously delayed, so that the tolerably long latent period of the opening excitation may be observed directly without further artificial aid. Later on we shall encounter an analogous effect in the indirect excitation of muscle. The significance of these facts to the theory of current-action, and the law of polar excitation in particular, is as clear as possible, and can hardly require further exposition. They afford as direct and salient a proof that the electrical excitation of the muscle is a *polar* effect of current, as the previous experiments in time measurement; for if all the cross-sections of the intrapolar tract were simultaneously excited there could never be such an extraordinary disparity in the excitatory action of the two directions of current as is exhibited when a sartorius muscle that has been injured at one end, or chemically altered, is

traversed in its entire length by the current. We saw that excitation only remained unaltered when the effective electrode was at the uninjured end of the muscle; in other cases it can be altered in a positive or negative sense when excitability is locally increased or diminished. If the electrical excitation of a muscle is once admitted to be a *polar* effect of current, it cannot be doubted that the magnitude of both closing and opening excitation must increase or diminish, as the excitability

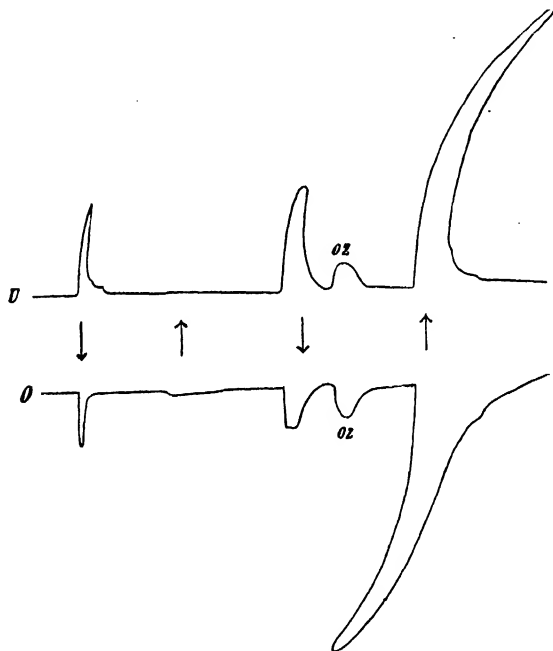


FIG. 89.--Twitch curve of sartorius fixed from the centre in double myograph. *a, b*, Normal; *c, d*, after treatment of one end with Na_2Cl_3 (upper end of the muscle). Enormous increase of the ascending closure twitch; opening twitch with weak descending currents.

of the contractile substance at the points where current enters or leaves the muscle, increases or diminishes. Whether excitability remains unaltered in all further sections of the muscle, or whether it alters in a negative or positive direction, is undoubtedly of great moment in the transmission of the excitatory process from its origin, but has not the remotest influence upon the intensity of the excitatory process discharged from kathode or anode. We may conceive a muscle with parallel fibres of equal diameter at both ends, having its cross-sections collectively

normal, and highly excitable, with the sole exception of the ends of the fibres on one side, at the point at which excitability of the contractile substance has been artificially lowered by any reagent; we should then be theoretically justified in the expectation that on sending current longitudinally through such a muscle, the effects of the closing, as of the opening, stimulus, would in a marked degree be found to depend upon the *direction of the current*, since the same stimulus would, in the one case, act upon normally excitable, in the other upon "fatigued," substance. In proportion as the local depression of excitability is higher at one end of the muscle, the more plainly would the difference in the excitatory action of the two directions of current come into evidence. And further, the extension of "local fatigue" cannot fail to affect the consequences of excitation, as appears from the following consideration. If we picture the muscle as divided into zones of equal magnitude, and assume that excitability is depressed in the end-zone only, while it remains normal in the others, it must obviously be possible to find a stimulus of the right strength to discharge an excitatory process in the former, which will propagate itself by conduction, and thus bring about a perceptible change of form, either in the entire muscle, or at least in the proximal half of it. But the same minimal stimulus will fail to produce this effect if the excitability of the zones immediately adjacent to the terminal section is depressed in the same proportion. For in such a case the excitation, starting with the same strength as before, dies out within a very short area, or gives rise to a weak persistent contraction only.

Such a muscle as we have been imagining can, in fact, be produced artificially. With careful exposure it results from treatment of one or other end of the sartorius with weak solutions of certain salts (*e.g.* acid potassium phosphate, and meat-juice, the effect of which is probably due to these salts), which do not essentially alter the structure of the immersed section of the muscle, but partially depress its excitability, giving the opportunity of determining the correspondence between experimental data and theoretical conclusions.

But the electrical current itself, by repeated closure with unaltered direction of current, induces still more completely a condition of the muscle, in which it reacts only in one,

and that the opposed, direction of current to the closure excitation, no external changes being perceptible. It can scarcely be doubted that this state also must be interpreted by local fatigue confined to the point at which current leaves the contractile substance, since there is no reason for assuming alterations of excitability in the intrapolar tracts, either positive or negative; while, on the other hand, it is indubitable that the excitatory process at the ("physiological") kathode occurs not merely at the moment of closure, but is also continuous, although as a diminishing quantity, during the entire passage of the current. It must therefore be taken as proven, that at least those tracts of the muscle, over which the persistent closure excitation extends, are more fatigued than the rest of the muscle, in which no manifestations of excitation can be detected during longer passage of not excessively strong currents.

The difference between local and general fatigue of a muscle is very pronounced when the response of a muscle fatigued by tetanus is compared with that of one that has been polarised by the constant current. Uniform stimuli (single induction shocks are best), whose efficacy for the normal muscle has been tested, are sent into different points, and the difference in height of twitch before and after fatigue determined. In the first case the excitability of the *entire* muscle will be much diminished, and entirely abolished for weaker stimuli (that had previously been effective), while a polarised muscle reacts to stimuli acting upon its continuity, as well as before the passage of the current, although the closure of a current, in the same direction as the "polarising" current, produces no sign of contraction, when it happens to coincide in its point of exit. From this we may conclude that the cause of failure of excitation in this case is to be sought in alterations localised at the point at which the current leaves the muscle-substance, or in close proximity to the same. This also appears from the effects of closing a current opposed in direction to the polarising current, when the excitation will be discharged at the point which was formerly the seat of the anode. The closure twitch observed under these conditions in the polarised muscle is considerably greater than before the passage of current (*voltaic alternative*). If this is correct, the effects of excitation by an induction current must vary according as it is sent longitudinally through

a normal muscle, or through one that has been polarised, care being taken in either case that the points at which the current enters or leaves the muscle are not altered. For since it has been established by time-measurements that weak induction shocks set up an excitatory process exclusively at the kathode, we may advantageously apply this fact in investigating the excitability of the kathodic end of a polarised muscle, by stimulating it through its entire length.

These experiments also demonstrate complete uniformity of response in a sartorius of which one end has been brought by the action of certain chemical substances into a condition of depressed excitability, and one that has been polarised by continuous passage of current with unaltered direction; the preceding discussion can be referred to in order to avoid repetition.

In conclusion, it should be remarked that the manifestations of fatigue after action of the constant current are usually the same as after injury to one end (heating or chemical destruction of a muscle), since in either case a graduated diminution in magnitude of the twitches can be observed before the total disappearance of the closure twitch, while the persistent closure contraction continues as long as possible. Little doubt remains therefore that the local depression of excitability—produced in the one case by the resulting continuous excitation at the point where the current leaves the muscle, in the other by a variously expressed chemical alteration of the muscle-substance—is the sole cause that the muscle is not at all, or very little, excited when the current enters or leaves it by the end thus affected, while in other cases both closing and opening excitations follow normally.

The following facts may be adduced as evidence of this proposition: in a preparation of sartorius it sometimes, though seldom, happens that the fibres remain contracted at certain definite points, so that an "idio-muscular" swelling rises up, now in the middle, and now at one or the other end of the muscle. The first case is the most frequent; whether it is connected with the hyper-excitability of the sartorius at the point where the nerve enters it, as remarked by Kühne, must remain a moot point. When the swelling is confined to the lower end of the sartorius, the longitudinal passage of the current expresses

itself by a marked reaction, *i.e.* only the ascending current normally discharges the make excitation, while the descending current, which is usually more effective, either produces no excitation at all (with medium currents), or excites in a much less degree than the ascending current. Hermann (28) succeeded in establishing this fact of "polar negative action" at the idio-muscular swelling on a still firmer basis, by experiments with cooled muscle. The same thing occurs where all trace of local contraction has already died out; for the latter disappears in some cases by itself, more especially when the muscle is immersed in 0.6 % salt solution. Here, as in the persistent closure contraction due to the constant current, a state of depressed excitability at the seat of the idio-muscular contraction must have intervened, from the partial continuous excitation consequent under certain conditions upon a mechanical excitation (extension), which is indeed a necessary consequence of the fact that every excitation is accompanied by metabolism.

We have already mentioned repeatedly that the response of a sartorius, of which one end has been killed mechanically or by heating, to the electrical current, can be satisfactorily interpreted on the hypothesis of a localised diminution of excitability at the seat of stimulation, and we have now to examine the data for this conclusion.

Since it is a well-substantiated fact that an uninjured muscle, surrounded on all sides by the sarcolemma, is excited each time an electrical current passes out at any point of its surface, and since, further, the nature of the conductor by which the entrance or exit of the current is effected is experimentally indifferent—apart from the unavoidable polarisation of metal electrodes—the response of a muscle injured at one end seems at first sight to be an exception to the general rule. Here we find that both the closing and opening excitation are usually wanting, or appear much weakened, when the current passes from living uninjured, into dead, muscle-substance, or *vice versâ*. It is easy to demonstrate that the dead contractile substance *per se* reacts to current like any other animal tissue (tendon, bone, etc.) that behaves as an indifferent conductor; the clay points of unpolarisable electrodes can be covered with dead muscle, and current led through them to the uninjured surface of a muscle, without causing any hindrance or difficulty to the excitatory process.

There must, therefore, in the continuity of a muscle, be some specific relation *at the limit between dead and living fibres*, which is capable of inhibiting excitation.

The simple experiment of reversal of current proves that the *total excitability* of the muscle is not injured by destruction of one end, but there is reason to suppose that excitability in the immediate proximity of an injured part is more or less diminished. This appears indeed to be contradicted by the experiment of bringing the epiphysis of the tibia (or of the pelvis, if the upper end of the sartorius is injured) into relations of conductivity with some point on the surface of the muscle, by means of a bridge of salt clay, beyond the injured part; the muscle will contract almost as sharply at closure of a descending (or ascending) current as before the injury: but it must be remembered that, according to all probabilities, the condition of acute depression of excitability is confined to the *immediate* proximity of the point injured; at all events this must occur immediately after the ends of the fibres have been crushed on the one side. That excitability *must*, generally speaking, *be diminished* at the border between dead and living fibres, follows from the fact that the process of dying invades the entire length of a fibre continuously, when once it has been introduced at any point; accordingly dead and living fibres are never in *immediate* juxtaposition, but the section of the muscle that has been structurally disturbed by the attack, and killed, must in the adjacent sections initiate every possible process of dying, and correlative state of excitability, as has already been pointed out by Hermann.¹

If it is true, as stated above, that the *extension* of "local fatigue" is important in determining whether an electrical stimulus of given magnitude does or does not produce change of form in the muscle, we may presume that the slow dying of one or the other end of the sartorius, on immersion in warm water, depresses the excitability of the muscle to one direction of the current more completely than simple mechanical injury: it cannot be doubted that the local, slowly-increasing effect of rising temperature is able to produce complete gradation of excitability in the sections of the muscle proximal to the section in heat-rigor. This view is confirmed experimentally (*supra*).

¹ Hermann, *Weitere Unters. z. Phys. d. Nerven u. Muskeln*. Berlin, 1867, p. 5 f.

The universal validity of the law of polar excitation being thus unequivocally established in the case of striated skeletal muscle, there is *a priori* no doubt of its further applicability to cardiac, as well as to smooth, muscle. In view of the structure of the heart (consisting, like all other smooth muscle, of innumerable cells in close juxtaposition, connected together by cement-substance), the question may fairly be asked, what — relatively to the previous definition — must here be understood by the “physiological anode or kathode?” To take a simple case, if we imagine a strip composed of parallel fibre-cells, as is approximately shown in a preparation of molluscan adductor muscle, we may expect such a preparation when traversed longitudinally by current to behave like a polymerous, cross-striated muscle, the several parts of which must be regarded anatomically and physiologically, as independent individuals. This is well exhibited in the *M. rectus abdominis* of the frog. If current is sent through this muscle, when it has been exposed and stretched between two corks, there is, as might be expected, at and during closure, on the anodic side of each tendinous intersection (if examined with transmitted light under the magnifying lens) a clear and sharply-delimited swelling of the ends of the fibres corresponding with the persistent kathodic closure contraction. It disappears at the moment of breaking the circuit, eventually making way for persistent anodic opening contraction on the other side of the intersection. It follows of course that the closing and opening twitch of each part must proceed from the same point.

The whole segmented muscle-band will thus be excited at as many points in its continuity as it has divisions, since each element of the muscle circuit has its kathode and anode respectively. And if the adjacent cells of the heart, or any other smooth muscle, conduct themselves like the constituents of a polymerous muscle, and if the interstitial, or cement, substance plays the same part as the tendinous intersection, it may be presumed that the electrical current will produce excitation at closure (or opening) at as many points in the continuity of the tract as there are cells present. For obviously the latter would each have their proper kathode and anode, so that, in consequence of the inferior length of the cell elements in question, the excitation (contraction) would in fact begin simultaneously at

innumerable points of the whole area traversed. Experimentally, however, the reaction of such a muscle, constructed of uninuclear cells, in no way corresponds with this theoretical process. We have learned from Engelmann's classical experiments that the ureter, like the heart, conducts itself *re* both transmission of the excitatory process, and polar excitation by the electrical current, "like a single, gigantic, hollow muscle-fibre." This proves once more that the cement substance does not separate the cells by forming indifferent partition walls, but actually, as it were, brings about the continuity of the substance. A series of muscle-cells, with the ends abutting on each other, and traversed longitudinally by current, would react towards it as a single muscle-fibre, and the connective substance would no more form secondary kathodes and anodes than the transverse discs within the striated fibrils. *In the one case, as in the other, there is physiological continuity of substance.* This can be proved experimentally, both in cardiac, and in various instances of smooth, muscle. If the ventricle, separated from the auricle, of the frog's heart (the "cardiac apex"), is used as the object of experiment, the asymmetrical form of the preparation entails the same result as in the sartorius, *i.e.* the density of current on direct application of the electrodes to either end (apex and base) is very unequal. It is therefore advisable to immerse the apex, according to Engelmann's method (27, p. 201), in an excitation chamber filled with indifferent fluid, so that there is approximately equal current-density at every point of the preparation, so long as the current is passing. Engelmann employed a glass vessel 13 cm. long, 4 cm. wide, and 3 cm. high, filled to about $1\frac{1}{2}$ cm. with a dilute solution of NaCl (0.5 %) and gum arabic (2 %), which the electrodes dipped into. On closing a battery current, or sending in a single induction shock, it is found that if the long axis of the ventricle lies parallel with the lines of current, the cut surface being vertical to the same, ascending currents (*i.e.* from apex to base) fail to excite immediately, or soon after making the section, or at least excite less effectively than descending currents. After a few minutes, however, the excitability to ascending currents reasserts itself, and rapidly increases, sinking again to zero if the section is freshened. The same dependence of excitation effects on direction of current appears also after injury to one or the other lateral surface of the

preparation, provided it is so arranged that the cut surface is perpendicular to the direction of current.

For the sake of brevity, we may, with Hermann, denote the direction of the exciting current which lies towards the cut surface "*atterminal*" ("*admortal*"), the other as "*abterminal*" ("*abmortal*"). The reaction observed may then be shortly expressed as follows:—*Immediately after injury to the cardiac apex, the closure of atterminal currents is ineffective, while under similar conditions the closure of abterminal currents is excitatory.* Obviously we have here a complete analogy to the response of the sartorius of which one end has been injured (or otherwise chemically altered), and the same conclusions may be deduced in both cases. In the first place, experiment proves convincingly that the contractions of the heart with electrical excitation proceed exclusively from the spot where the current passes from the living muscular tissue into the foreign medium beyond it, whether this is salt solution or dead muscle-substance. This represents the *physiological kathode* of the preparation, and here alone can the make excitation originate. On this presumption only does the effect of local injury upon excitability to closure of atterminal currents, with failure of effect upon excitability to abterminal closure, become intelligible. It holds good, however, for the apex of the heart, which consists of innumerable irregularly fused cells, just as much as for the approximately parallel-fibred monomeric sartorius.

In both cases the excitation propagates itself at closure over the whole surface of the muscle, from its point of departure, by conductivity (from cell to cell), the exact seat of the kathode on the surface of the preparation seeming to be quite indifferent, while the excitability of the points affected has, on the other hand, an important influence on the consequences of excitation. If the current leaves by an injured point, excitation takes place at a less excitable spot, and the effects can be interpreted just as in sartorius, under similar conditions. The only noticeable difference is the rapid restoration of normal reactions. Engelmann explains this naturally by the assumption that the single cells, though connected by relations of conductivity with their neighbours while living, *die* singly, each to itself; in other words, the process of dying does not pass over from cell to cell like that of excitation. Where the superficial cells are quite dead,

the kathode no longer falls at the limit of moribund, *i.e.* less excitable, muscle-substance on the one hand, and surrounding fluid or dead cell-substance on the other, but lower down at the border of living and dead cells, *i.e.* at the demarcation surface. Every polymerous striated skeletal muscle, as can easily be demonstrated, exhibits the same reaction. The consideration of the electromotive action of the heart (*infra*) further confirms this theory. Another method of demonstrating the law of polar excitation on cardiac muscle, when it is totally uninjured and remains in diastolic relaxation, is the so-called *unipolar stimulation*. Since excitation by the electrical current depends in the first place upon its density at the point of ingress or egress, it is *prima facie* evident that the diminution of the same at one pole, with simultaneous maximal increase at the other, may furnish an explanation of the law of polar current action. Thus, indeed, as was pointed out by Kühne (28), we may obtain an electrical excitation as weak as that formerly produced by mechanical excitation. If two punctiform leading-in electrodes are imagined upon the surface of any conductor, the whole interior of the same will be traversed by lines of current, whose density is greatest at the point of contact, and slowly diminishes outwards. And if by employing a flat electrode, the density, and consequently the efficacy, of the current is rendered minimal, or negative, at the point where it enters, or leaves, the muscle, the other electrode only will finally remain effective at the point of contact, and may, as it were, be localised by limiting the surface of the contact as much as possible. If, for example, the skin is removed from the ventral surface of the thigh of a curarised frog, the broad surface of one (the indifferent) electrode being applied to the skin of the throat, while the other, the finest possible pencil electrode, is in contact with any point of the moist surface of the muscle, characteristic effects of excitation appear, which differ widely, according as contact is effected at the kathode or anode. In the first case, on sending in a weak current, the bundles of fibres immediately under the point of the electrode may be seen to contract at the moment of closing the circuit, producing for a moment a small longitudinal furrow on the smooth, even surface of the muscle, while at the actual point at which contact is effected a small, sharply-defined transverse swelling appears, which—provided the contact is unbroken—

persists unaltered throughout the entire period of closure. We cannot doubt this to be a persistent kathodic closure-contraction. If the intensity of the excitation current is strengthened, both the twitch and the continuous contraction increase also, although the latter never loses its localised character. This appears most clearly if (as above) marks are affixed to the surface of the muscle, which, by moving in opposite directions during contraction, are a measure of its spatial extension. The muscle investigated may, *e.g.*, be painted with sepia bands at right angles to the direction of the fibres, so that the distance between each two lines, drawn with a fine bristle, is about $\frac{1}{2}$ mm. Every contraction thus defined expresses itself therefore by a more or less conspicuous decrease in one or several cross-bands, or the uncoloured spaces between them. Within those tracts of the muscle, on the other hand, which are only passive factors, the coloured cross-bands, though variously distorted, do not become smaller. It is undeniable that with the unipolar method of excitation, as described (where the lines of current do not, generally speaking, pass in and out through the natural ends of the muscle, but traverse the fibres in the most opposite directions, oblique and transverse,—which must partially affect the current action), the conditions of experiment are less easy to summarise than with the customary bipolar method, and the results, *e.g.*, in regard to the possibility of action from secondary kathodic or anodic points in the proximity of the exciting electrode, often hard to interpret. Still this method has its advantages in many cases where the bipolar method could not well be brought into application. This occurs emphatically in many smooth muscular parts, and not less in cardiac muscle, where the complex and intricate course of the fibres makes it *a priori* impossible for the current to traverse all the individual elements longitudinally. The cells thus fitted together in all conceivable directions would more probably be traversed by the lines of current in the most various directions, and at widely-divergent angles. But as shown by the above, this is of little importance to the final consequence. If the ventricle of the frog's heart is arrested in diastole, according to Bernstein's method, by squeezing it away from the auricle, it appears filled out with blood, and reacts to every mechanical stimulus by a powerful total contraction. If, once more, the broad electrode

of the battery current is applied to any indifferent part of the frog's body, while the other is in contact with the surface of the ventricle, the closure of the circuit will, on stimulating with a just effective current, without exception excite only when contact with the heart is made by the kathode, never when it is formed by the anode; sometimes, however, the opening (at least after a long closure) will also be effective. And if the validity of the polar law of excitation is thus incontestable for cardiac muscle, it can be demonstrated in appropriate cases for smooth muscle also.

As such, we may refer, *inter alia*, to the adductor muscle of Anodonta, of which the response to current has already been frequently quoted, and which, from its generally-speaking regular and parallel-fibred structure, presents the best comparison with the frog's sartorius. It was said above that a preparation of the adductor muscle, as free from tonus as possible, persists in a shortened state during the entire passage of the current. The merest inspection will suffice to show that neither at closure nor opening (where the latter is effective) of the current does the *entire* intrapolar tract become persistently and uniformly contracted, but in the first instance the kathodic, in the second the anodic, half will be mainly affected. Undoubtedly this is a phenomenon analogous with that of the transversely striated frog's sartorius, where the corresponding localisation of the closing, or opening, persistent contraction has long been known, and has always been regarded as substantial confirmation of the law of polar excitation by the electrical current. More exact conclusions are obtained from the application of the graphic method recording the separate contraction of either half of the muscle, which is possible here as in the sartorius, by fixing the centre of the muscle. But while in striated muscle, as a rule, at the moment of closure, as also eventually at break of the current, a wave of contraction is propagated from the kathode, or anode, with great velocity through the entire length of the muscle, producing on either side of the fixed centre an approximately equal twitch at closure or opening, in molluscan muscle we find only a more or less localised persistent contraction, corresponding with the persistent closing and opening contraction of striated muscle, which, like these, fails altogether if the entrance or exit of the current is effected by a layer of dead con-

tractile substance (3). Of this the accompanying curve (Fig. 90) gives sufficient evidence. As in cardiac muscle, the striking disparity of effect between the two directions of current immediately after the injury equalises itself by degrees, and at last becomes imperceptible. The explanation here again must be sought in the independent dying of each fibre-cell.

If these conclusions from the adductor muscle of *Anodonta* are in almost complete conformity with the polar effects of current in striated skeletal and cardiac muscle, this is not equally true of other parts composed of smooth fusiform cells, in which excitation with the constant current provokes a series of manifestations differing in many respects (at least at first sight) very widely,

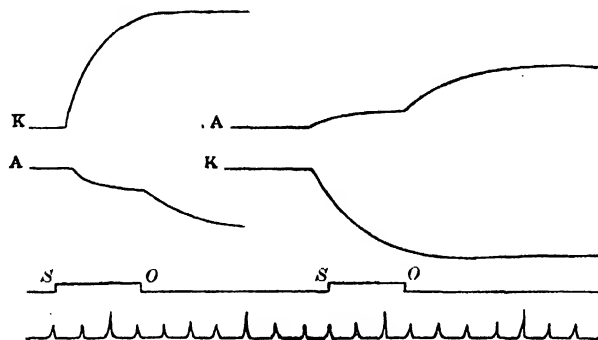


FIG. 90.—Localisation of persistent closure contraction at the cathode (*K*) on exciting the adductor muscle of *Anodonta*. *S*=closure; *O*=opening.

and thus suggesting that the polar law of excitation may not be rigidly applicable to all kinds of muscle (31).

Within the integument of *Holothuria*, along the entire length of the body, there is a beautiful series of longitudinal muscle-bundles, with parallel fibres, in the form of five flat bands, composed of solitary spindle-cells, pointed at either end, which, after the animal (*H. Poli*) is opened, appear as pale, or pinkish, and transparent striæ. Many thinner and finer bands of circular muscle run between each two longitudinal muscle-bands, forming a complete investment of the body at right angles to the latter, and, like them, consisting of spindle-cells. In the muscular integument, when split up lengthways, and properly stretched, the longitudinal muscle-bands may easily be isolated in their whole length, or in portions only, by passing a probe under one

end of the muscle and pushing it along the muscular band, pressing it against the attachment. Excitation experiments can then be tested on this isolated and freely-stretched band of muscle, just as in the muscle of Mollusca. In every instance the protracted tonic contraction into which these muscles usually fall, more especially after mechanical injury, is very disturbing; but after a period of rest under sea-water relaxation sets in again sufficiently to make experiment possible; a certain degree of tonus, however, persists and must be taken into consideration. If two fine pencil electrodes are then applied simultaneously to two points, not too close together, of a longitudinal muscle-band, lying *in situ* or stretched between two corks, or if one electrode is laid on some indifferent part of the preparation, the other only being in contact with the muscle, there will, in either case, be characteristic changes of form at the points where current enters or leaves the muscle, differing widely at the two poles (29).

As soon as the circuit is closed, a small transverse swelling arises at the kathode, exactly under the electrode in contact, and extends thence at right angles to the direction of the fibres; under some conditions (not too weak a current) this swelling spreads over the whole breadth of the muscle-band, and stands out sharply from the region round it. This "idio-muscular," kathodic swelling persists during the period of closure, and (what is specially remarkable) never spreads beyond the point where it originates. The total shortening of the muscle-band produced by the localised contraction is always insignificant, since it is essentially only the part of the muscle immediately adjacent to the exciting electrode which contributes to the local expansion. It also depends, of course, upon the strength of the current used for excitation, so that within a certain range the kathodic swelling, which undoubtedly corresponds with the persistent closure contraction of striated muscle, increases with the strength of the current, and then includes a larger tract of the muscle. With very weak minimal currents the upper layers of fibres only contract locally, so that the kathodic swelling does not extend over the whole thickness of the muscle. In all cases the sharp delimitation of the kathodic continuous contraction is very remarkable,—it rises in a crest, descending sharply on both sides to the surface of the muscle.

The excitation effects produced under similar conditions at the point where the current enters are quite different. Here at the point where the anodic electrode is in contact with the smooth, even surface of the muscle, a more or less profound canal or furrow arises at make of the current, and runs transversely over the muscle; its length and breadth correspond more or less with the transverse swelling, which appears, or (with unipolar excitation) would have appeared, under the same conditions at the kathode. It is easy to see that the bulk of the muscle is pushed over from the anodic side at the moment of closure, and, as it were, flows away, while on either side of the hollowed canal a swelling rises up, of similar aspect to the kathodic continuous contraction. The changes of form in the muscle which ensue may therefore be characterised as a deep hollow, rising up under the electrode, marked off on either side by a transverse swelling.

Under certain conditions yet to be considered, it appears as though the two swellings were formed solely from the muscle-substance dragged away from the anode. But if the experiment is made with fresh, excitable preparations, it will be found, without exception, that a conspicuous contraction appears on both sides of the anode, and extends over comparatively wide tracts of the muscle; it is most evident in the immediate proximity of the hollowed canal, and decreases on both sides of it. In other words, at make of the current the muscle elongates itself close to the anode by relaxing, while in consequence of the excitation produced in the surrounding region, the muscle-substance presses in towards the relaxed point. In this way there is often for the whole muscle a more considerable, and always much more important, shortening, than in kathodic excitation.

Since the flat longitudinal muscle-bands of *Holothuria* are tolerably broad, the excitation effects described above can only appear in one part of the fibres, when the electrode points are applied to the centre of the muscle. The changes of form are, however, much more striking, and can be seen at a greater distance, if the muscle is lightly stroked with the brush electrode at right angles to the direction of the fibres.

The same manifestations (as on the electrical excitation of the longitudinal muscle-bands) appear in the thin bundles of the circular muscles, although they are less striking owing to the greater delicacy of structure. If a perfectly level point of the

surface is brought into contact with the kathode, a small longitudinal swelling springs up under the point of the electrode as soon as the current is made, its long axis lying perpendicular with the course of fibres in the muscular bundle excited. The whole manifestation is indisputably the same, in a less degree, as the persistent kathodic contraction when a longitudinal muscle-band is excited.

In both cases there is the striking demarcation of the swelling, as well as the inconspicuous total contraction of the muscle, due to local excitation. In contrast with this, the total contraction of the ring-muscles is very marked with unipolar stimulation from the anode. Careful gradation of current and a fine-pointed brush electrode are essential in order fully to determine the contrast of excitation effects in circular and longitudinal muscles in this case also. If a single bundle of circular fibres is excited in the middle, between two longitudinal muscle-bands, the most striking appearance on closing the current is the formation of a furrow running parallel with the direction of the fibres, the origin of which is easy to explain from the sharp contraction of the excited fibres. With artificial enlargement, it is easy to see that the muscle-fibres immediately under the point of the anode do not take part in the contraction, but (as in longitudinal muscle under corresponding conditions), a more or less well-marked canal is formed, running transversely to the fibres, at either side of which the muscle-bundle shortens. Sometimes the transverse swellings which mark off the canal on either side stand out quite clearly; yet it always requires close observation to detect an appearance, which is obvious when the longitudinal muscles are excited. While in the latter, with anodic excitation, total contraction tends to disappear in favour of local changes of form owing to the great length of the muscle-bands, the exact opposite occurs in the small short bundles of circular fibres, in which the total effect is more striking than the local changes. This is best studied at points where, from the contraction of the surrounding parts and consequent folding over of the membrane, or from pronounced total relaxation, individual parts stand out in a blister. If contact is made with the anode at such a part, where the circular fibres appear curved convexly outwards, closure at once produces a segmental constriction, parallel with the fibres, and recalling the similar effect produced under analogous

conditions in the intestine, more particularly in the colon of *Herbivora*. This, however, obviously makes any exact investigation of the local changes arising at the point of contact itself as good as impossible. With kathodic stimulation, on the contrary, they are very apparent, inasmuch as a small, but sharply-defined, transverse swelling is formed, with only minimal total shortening at the point where the current leaves the muscle.

The smooth masticatory muscles of *Echinus esculentus* exhibit a no less remarkable and characteristic response to electrical excitation with the galvanic current, the reactions, moreover, being much more rapid than in *Holothurian* muscle (29). The calcareous skeleton of the so-called lantern of Aristotle consists of five symmetrical segments, each again consisting of several pieces. The segments are joined together partly by bands, partly by very strong muscles, which are partially very regular in structure. This is in particular the case with the five very short, but quite parallel-fibred muscles, which at the inner basal surface of the lantern connect the five, long, movable chalk ribs, that run out radially from the central oesophageal cavity towards the periphery, where they curve down over the lateral surfaces of the lantern. Besides these five muscles, which form a closed ring, and are each, in large specimens, 1.5 cm. long, and about 4 mm. broad, the other larger muscles, which are inserted into the jaws, and move the teeth set into them, and also fill up the intermediate space between, are very convenient for experimental purposes. No especial preparation is necessary for the first orientation experiment. It is sufficient to divide the sea-urchin with scissors into an upper and lower half, breaking away as much of the shell from the oval part containing the lantern as will give convenient admission to the electrodes. After drawing the teeth with forceps, the membranes that partly cover and partly connect the muscles must also be removed, and the preparation is then sufficiently ready for experiment. If it is now dipped in a vessel of sea-water, which is as indifferent for these muscles as for those of *Holothuria*, so that only the base of the chalk pyramid with the ring of muscle projects freely, and any point along any one of the five muscles is brought into unipolar contact with the fine-pointed kathode, while the other unpolarisable electrode dips into the water of the vessel, the formation of an idio-muscular swelling will be even

more elegantly demonstrated than in the longitudinal muscles of *Holothuria*. With appropriate gradation of strength of current this appearance can be seen at every possible stage of development. The transparent nature of the smooth thin muscles, as well as their promptness of reaction, are very favourable, and it would be difficult to find any other object in which the local manifestations of excitation at the kathode can be so elegantly demonstrated. The contracted part stands out with extraordinary sharpness and plasticity from the surrounding region as a pale opaque bleb with a peculiar dull lustre; it rises quickly upon closure of the current, remains unchanged during its passage, and only sinks down again gradually when the circuit is opened. If a minimal current is used for excitation, the contraction appears more and more localised to the immediate proximity of the point of exit, gaining in amplitude with increasing intensity of current, until finally the kathodic bleb at the electrode spreads over the whole extension of the muscle in the form of a knotty swelling, and as the muscle-substance is, as it were, drawn up on either side to form this swelling, a not inconsiderable shortening of the entire muscle follows. But it is never so strongly marked as with unipolar anodic excitation.

In this case, when the current is closed, a marked total contraction of the whole muscle makes its appearance, so that the movable points of insertion are brought as closely together as possible.

The muscle appears tensely stretched, and at first seems to be uniformly shortened at every point. This last effect is very striking in view of the reactions previously described for kathodic excitation. There is in consequence not merely no strong local contraction at the anode, but on applying somewhat stronger currents there is an actual interruption of continuity in the muscle. If the electrode (anode) is brought into contact with any point of the free, sharp edge of a muscle, the latter extends itself considerably at closure, and before long a thin transparent point will appear at the electrode (under the magnifying lens), upon which the fibres next in contact to it break away, and curl back on either side. If the electrode is advanced the whole muscle will sometimes break up transversely, the fibres breaking away from the part in contact, in proportion as the layers are disturbed deeper and deeper.

The key to this somewhat startling fact seems to lie in the reaction of the Holothurian muscles, as described above. We can hardly doubt that in both cases there is complete conformity in regard to kathodic effects of excitation. But even the seemingly divergent effects in unipolar anodic excitation of Echinus muscles, must really be traced back to changes analogous with those so clearly expressed in the longitudinal muscles of the Holothurians. Here at the very entrance of the current we found a local relaxation, marked by the formation of an attenuated part from which a contraction that is well marked in fresh specimens develops on either side, and produces a considerable total shortening of the muscle. Now if a short, fine muscle of identical or similar properties were stretched between two points of insertion, which in contracting can only be approximated within certain limits, the effect of the kathodic closure excitation would obviously be the same as in the yielding attachment of a Holothurian muscle.

With unipolar anodic excitation the effect is, however, quite different. If the current enters at any point along the muscle, and local relaxation appears after closure, or if the part in contact remains unexcited while a marked contraction occurs on either side of it, there must obviously, if the point of insertion cannot be further approximated, be an interruption of continuity at the point of least resistance.

The tearing apart at the anode would on this assumption be referred to the fact that in unipolar anodic excitation of the muscle, relaxation occurs at the contact itself, but there is a marked condition of tension on either side if the muscle, on account of the given mechanical conditions, is unable to contract further. This is also the reason why Echinus muscle stimulated *in situ* does not, like Holothuria, exhibit a deep canal with walls rising round it at the anode, but only a tension which is apparently uniform at every point.

The two last cases also interpret those more complicated instances, where, *e.g.*, in the muscular integument of many worms, and also in the intestine of vertebrates, two systems of smooth muscle-cells lie superficially directly over each other, so that the direction of fibres in both is at right angles (30). If a large earthworm, paralysed with dilute alcohol (5 to 7 per cent), is placed on a leading-off stage, which is constructed of several layers of

filter-paper or salt clay, and is in contact with one (the indifferent) electrode, while the other (a fine brush electrode) is placed on the centre of the dorsal surface of one of the broad segments at the anterior end of the worm, a sufficiently strong current—given maximal paralysis of voluntary movements and reflexes—will throw the segment in direct contact (and that segment only) into circular constriction, in which state it will persist as long as the current remains closed. If the current is strong and the excitability of the muscle high, this constriction (produced by contraction of the circular muscles) may almost obliterate the lumen of the body-cavity, thus of course producing more or less passive distortion of the surrounding parts, and of the immediately contiguous segments in particular. The excitation effect, however, remains localised in the segment in direct contact, and there is no propagation of contraction in the form of a peristaltic wave. But along with this passive contraction of the adjacent portions of the muscular integument, there is rarely wanting an active decrease in height of the contiguous segments, due to the contraction of the longitudinal muscles, which is most strongly marked in the immediate proximity of the constriction, and gradually diminishes outwards, so that it is never perceptible at the whole periphery of the segments affected, but only at the side corresponding with the seat of excitation. Hence we must be dealing with a unilateral contraction—mainly active, but in part passive also—of the body-rings adjacent to the anodically excited segment. The proof that this is a genuine shortening of the longitudinal muscles (apart from the spatial extension of the changes produced at either side of the circular muscle contraction, which may be very considerable) lies unquestionably in the important decrease in height of the segments affected, and the only doubtful point is how the directly excited segment itself reacts under these conditions. It is *prima facie* evident that there is an often maximal excitation of the circular muscles, while perceptible shortening of the longitudinal muscle on the other hand is everywhere absent. This cannot perhaps be determined only from the fact that there is no apparent decrease in the height of the muscle-segment concerned, since the two layers of muscle work antagonistically both in regard to changes in length (height), and in breadth, of the segment, but on the other hand it is indisputable that cases may be observed

in which the contraction of the circular muscles is comparatively less developed than the contraction of the longitudinal muscles, on either side of the ring in contact with the anode, so that the latter is only constricted in an inferior degree; nor does the height of this segment diminish, although this is in a marked degree characteristic of the neighbouring segments. Moreover, there is another feature in every case, which seems to be of importance in the conception of the anodic effects of excitation.

If the contraction of the circular muscles is pronounced, the excitation appears to be developed with approximate uniformity at every point of the muscle-ring, as though the process of excitation, *i.e.* contraction, starting from the anode, was transplanted on either side from section to section. This idea at once suggested itself from an unprejudiced consideration of the effects of excitation. But if the ring-shaped constriction is not maximal, so that the part of the segment in contact with the anode remains visible, it can usually be seen (at least under the magnifying lens) at the actual point where the current enters, as well as in the immediate proximity, not only that the contraction of the longitudinal muscle is wanting, but that there is not even any perceptible contraction of the circular muscles. This is especially plain when the surface of the worm has dried from evaporation, and consequently become less elastic. It then appears very elegantly that fine cross-wrinkles arise from the involution of the epidermis on the surface of the contracted ring; these are plainly visible at either side of the electrode, but fail altogether in the immediate proximity of the anodic contact. The electrode must be only just moist in this experiment, so as to avoid wetting the seat of excitation. In every such case a directly relaxing (inhibitory) effect of the anode may be demonstrated, if the contact is pushed, during closure of the current, towards any point of the excited segment in which the contraction has already produced obvious transverse wrinkles. As soon as such a spot is brought into contact with the anode it begins to smooth itself, and gives the impression that—notwithstanding the contraction of adjacent parts of the muscle-ring—relaxation and lengthening occur at the actual seat of contact. It is by no means rare in longitudinal as in circular muscles, to find this failure of contraction at the anode itself, still more plainly marked by

the formation of a little superficial dint or hollow, the origin of which can be easily explained. It is obvious that when no excitation occurs at the point at which two muscle bundles of equal breadth cross at right angles, while, on the other hand, the arms of the cross beyond the juncture do contract—the more strongly in proportion as the section is applied nearer the crossing point—a quadratic hollow, bordered by four large swellings of equal dimensions, must be developed. An exact diagrammatic representation of this effect in the excited segment of the worm is from anatomical reasons obviously impossible, but it can often be seen that the segment in contact with the anode is drawn in at that point, and appears to be surrounded by bulging walls, which must be referred partly to the portions of the circular muscles contracting upon themselves in the segment, partly to the equally shortened longitudinal muscles of the next adjacent segment.

The whole effect can often be brought out more strongly if, with the current closed, two contiguous segments are repeatedly stroked at right angles to the direction of the fibres with the brush electrode, upon which both the unexcited surface and the area of contraction become larger, and stand out more sharply from one another.

Most convincing of all, however, is the local inhibitory effect of the anode (*supra*) at those points, where either the longitudinal or circular muscles, or both, seem for some reason to be permanently contracted. The local relaxation of both systems of fibres at the segment in direct contact is then very plain, and quite unmistakable.

The changes at the kathode are no less striking than at the anode, when the muscular sheath of *Lumbricus* is excited electrically during closure. It would almost be sufficient to say that they express themselves by a direct antagonism, but it is advisable to describe them a little more in detail.

If attention is directed solely to the segment in contact with the electrode, the antithesis of the anodic and cathodic excitation effects is very striking, and would (without minute examination) suggest that with closure of current at the anode the circular muscles, at the kathode the longitudinal muscles, are exclusively excited.

It has already been shown, however, that the relations are by

no means so simple at the anode, nor are they more so with kathodic excitation. There can be no doubt that the longitudinal muscles of the directly stimulated section are excited, but we may question, for reasons to be stated below, whether the ring-muscles are not also, at least locally, excited at the point of contact.

The first desideratum, in an exact observation, is not to employ too strong a current, since the problem will otherwise be unduly complicated. It must be remarked once more that the results of bipolar, coincide exactly with those of unipolar, excitation. The more striking change is, as we have seen, the shortening (decrease in height) of the body-rings implicated. This is not, as a rule, uniform throughout the periphery, but is essentially confined to the immediate proximity of the kathode. Here, in consequence of the longitudinal muscular contraction, the segment involved appears in relief as a swollen blister, between the contiguous segments. The latter participate equally in the stimulation with stronger currents, so that on closure of the current the longitudinal muscular contraction, extending over several segments, causes a more or less pronounced swelling to spring up, which is mainly confined to the point directly excited, rises most abruptly under the kathode itself, and falls away tolerably quickly on either side of it. If the tract of kathodic excitation is examined at an appropriate strength of current, with a magnifying lens, particular attention being given to the appearance of excitation effects in the segment directly in contact with the electrode at the moment of closure, it is not usually difficult to ascertain positively that there is also at that point a contraction of the circular muscles, localised to the kathode, which only remains unnoticed with less attentive observation, because its spatial restriction prevents any perceptible diminution of diameter in the muscle-ring. This effect is limited, with the application of moderate currents, to the segment directly excited, and in consequence a marked, lumpy protuberance is often visible at the point of contact, which is no doubt due to the disguised and local contraction of the longitudinal and circular muscles. In order to attest the latter it is important to note that in the muscular integument the layer of circular muscles (conversely to the vertebrate intestine) lies externally, and is thus directly accessible to observation. Other-

wise it would be difficult to come to any conclusions as to the changes in the circular muscles, particularly with kathodic excitation (Fürst, 30).

We have so far been investigating the manifestations of excitation at closure only. It remains to add a few words as to the polar effects that appear on opening the circuit. As in most other cases, so here, it is found that stronger currents and prolonged duration of closure are essential to produce effective break excitation. It need hardly be added that individual differences of excitability in the preparation are also prominent factors. The opening excitation effects, at least in *Lumbricus*, are never so sharply defined as those at closure. The most definite appearance is a contraction of the circular muscles—similar to that of the anodic closure—at the previously kathodic segment, on opening the circuit; yet it is difficult to decide with certainty whether the contraction spreads itself in this case, as in anodic make excitation, on either side of a relaxed point. Yet more difficult is it to determine the nature of the co-operation of the longitudinal muscles, as appearing under certain conditions after strong anodic excitation of a segment on breaking the current. It is partly due to the comparatively slow equalisation of the excitation effects after closure, which—at least sometimes—produces a superposition of what may be taken as the antagonistic effects of closing and opening the current, by which the question is further complicated.

The effects of electrical excitation in the leech, and in *Arenicola* (29) in particular, are quite as characteristic as in the muscular integument of the earthworm. Here, too, the most prominent effects at closure of the current are, on the one hand (at the anode), contraction of the circular muscles of the segment directly in contact with the electrode; on the other hand (at the kathode), the marked shortening of the same in consequence of the contraction of the longitudinal muscles. Owing to the small distance between the transverse furrows which encircle the worm's body, the kathodic effects of excitation spread, more particularly in the leech, over a large number of segments, whilst in a long body-ring, *e.g.* at the anterior end of *Lumbricus*, the kathodic contraction of the longitudinal muscles (at least with weak excitation) is often only segmentally developed. The flat shape of the body in the leech, moreover, brings out plainly the localisation of effects of kathodic excitation to the dorsal surface excited.

There is never an undulatory transmission of the contraction over large sections of the worm-body. On the contrary, these remain fixed in the expansion determined at closure as long as the current is passing, and this applies as well to the anodic circular, as to the kathodic longitudinal, muscular contraction. In the leech also it is certain that the latter does not appear singly, but is accompanied by a simultaneous localised contraction of the circular muscles at the point of contact with the electrode. A small but plainly visible swelling accordingly starts up under the electrode, running transversely to the fibres of the circular muscles, and, as it were, opposed to the expansion produced by the contraction of the longitudinal muscles. No trace of excitation is visible in the same bundle of circular fibres beyond the small, sharply-defined swelling. Where a perceptible ("tonic") contraction existed already before closure, it may be seen to expand into the localised swelling at the point of current exit. At both sides of this there will then be a visible relaxation of the circular muscles, so that at times the lateral parts of the segment bulge out bladderwise, convexly to the exterior, thus producing a very characteristic, and more or less complicated, change of form in the muscular integument at the proximity of the electrode. The swelling caused by the local contraction of the longitudinal muscles is also sharply defined on either side, although, as stated, it extends over several segments. At break of the circuit the changes described (Fürst, *l.c.*) are either equalised simply, or (with stronger currents, and longer duration of closure) a break excitation makes its appearance, as in the earthworm, by a shortening of the circular muscles, which extends over large areas of the previously excited segment, producing a more or less pronounced segmental constriction—a change, of which the resemblance to the effects of anodic make excitation is *prima facie* evident, although it is difficult to demonstrate complete coincidence in the two cases. While on bringing any points of the upper surface of the muscular investment of *Hirudo* into contact with the kathode, there is, in consequence of the simultaneous shortening of the longitudinal and circular muscles, a general pressure of the muscle-substance from all sides towards the point where the current leaves the muscle, a precisely opposite effect appears with anodic excitation. It is even more evident in *Hirudo* than in *Lumbricus*, that the segment in contact with

the anode remains unexcited at the point of contact at the instant of closure, or relaxed if there has been a previous tonus. In this example a good indication of contraction, or relaxation, of the circular muscles is afforded by the relative distance of the fine transverse lines of the skin, through which each segment vertical to the direction of fibres in the circular muscles exhibits parallel striæ. At every shortening of the circular muscles, these striæ approximate at the contracted parts; at every extension the space between them gets larger. This last occurs unmistakably at closure of the current in the immediate proximity of the anodic contact, together with a marked contraction, and subsequent circular constriction, of the segments implicated. This also applies, at the same point, to the longitudinal muscles, which do not shorten at the electrode itself; the height of the segment does not alter. On the other hand, as in the earthworm, a more or less extensive contraction of the longitudinal muscles appears in the segments implicated on either side of the circular constriction, in proportion with the strength of the current; this is most developed in the immediate vicinity of the body-ring in contact with the anode, and gradually decreases outwards.

All these facts combine to show that the so-called smooth muscles of very different invertebrate animals exhibit, as regards their reaction to the electrical current, a wide, almost complete, uniformity of behaviour. Here, too, the law of polar excitation prevails in general, although certain effects appear which are apparently without analogy in striated muscle. As a general rule, the proposition still holds that at closure of a sufficiently strong current, excitation and contraction follow at the physiological kathode. Where at first sight there seem to be exceptions (*e.g.* in the circular fibres of the muscular integument of worms), more exact observation brings them under the same law. Especially notable is the fact that *the kathodic closure excitation is localised in every instance to the point of exit of the current, and its immediate proximity, in the form of a local "idio-muscular" swelling (persistent closure contraction).* In no case is an undulatory propagation of the contraction to be detected.

Further, in conformity with the law of polar excitation, *there is at closure of the current no localised excitation at the anode, but rather an inhibition of a previously existing condition of excitation, while an opening excitation, on the contrary, does occur*

at this point, under some conditions. That, notwithstanding, a frequently well-marked total contraction of the muscle bundle should almost invariably occur with unipolar anodic excitation, is because the fundamental excitation at closure of the current does not proceed from the anode itself, but originates in the region proximal to it, as will presently be described. This accounts for the somewhat surprising fact that closure of current at the anode, in electrical excitation of the worm's integument, produces a (sometimes maximal) constriction of the segment in direct contact, and also accounts for the marked shortening of Echinus and Holothurian muscles in unipolar anodic excitation, as well as the no less striking rupture of the former at the spot at which current enters.

From this point of view it is easy to explain the excitation effects in the intestine of invertebrates (31)—at first sight so unexpected and irregular. If a given surface-point of a quiescent loop of the small intestine of any mammal is brought into contact with the anodic electrode, at sufficient intensity of current, while the kathode is again applied to any indifferent part of the body (liver, stomach, etc.), a circular constriction is formed, as in worms, and may, under some conditions, lead to the complete closing up of the intestinal tube at the point in question. This contraction persists throughout the duration of closure, provided the latter does not extend over too long a period, and equalises itself again without much delay when the current is broken. This effect of excitation can be very well seen in loops of the intestine that are moderately extended by fluids or gases. Provided the exposed intestine is not unduly cooled, and is still highly excitable, there will at closure of the current, in addition to the local contraction of the circular muscles at the anode, be a more or less evident peristaltic, or anti-peristaltic, movement in the proximity of the point directly excited, of which in this case it is hardly possible to say whether it is directly caused by a branch of the current, or is carried on from the primary seat of excitation. We shall see later that under certain conditions the anode does actually become the point of departure of peristaltic contractions spreading on either side, while in other cases a merely local constriction appears. Various sections of the intestine in this respect give a uniform reaction, and at most show differences in degree, which are due to the unequal develop-

ment of the circular muscle layer. Thus in the thin-walled and usually replete colon of *Herbivora*, the constriction does not usually include the entire periphery, but only forms a few, or several, deep segmental furrows.

The effect is very different on reversing the current with cathodic excitation of the intestine. We cannot entirely follow Schillbach, who first investigated the effects of electrical excitation of the intestine, when he speaks in this case briefly of a local contraction, and only sees as an essential difference in the working of the two electrodes that there is an appearance "at the anode of peristaltic waves, particularly in an upward direction," while at the kathode, on the contrary, the contractions are wholly local. For, on the one hand, the appearance of a contraction limited to the seat of direct excitation is very general at the anode also; while, on the other, it must be admitted that the visible effects of excitation at the seat of the kathode always exhibit a fundamentally distinct character from the effects of excitation at the anode. While the typical circular constriction is never wanting at the anode, and appears similarly at the small intestine, as well as at the colon, or rectum, the manifestations of excitation at the kathode develop very variously both in different species of animals and in different intestinal sections of the same animal. In rabbits, guinea-pigs, and mice, complete constriction of the tube of the intestine occurs at the anode, on closure of the current, while at the cathodic contact the change is scarcely perceptible, and it is only by very exact observation that the formation of a small, fluted thickening can be detected, and, corresponding with it, in its immediate proximity, a flat, dented constriction of the upper surface. This longitudinal fluting, which is only indicated at the point where the current leaves the intestine of rabbits or guinea-pigs, appears invariably in that of cats or dogs as a crest-like, prominent expansion, parallel with the long axis of the intestinal canal, and, like a scar, producing constriction of the tract lying immediately around it, so that on that side of the intestinal wall a flat, dented depression is formed, with the fluting already referred to springing from its centre. These changes also persist during the closure of the current, and only equalise themselves more or less rapidly when the circuit is broken. The manifestations of polar excitation in the different sections of the colon of *Herbivores* are also interesting—the anatomical

arrangement of the muscular layers presenting unmistakable analogies with the relations described in *Holothuria*. In neither case do the external longitudinal muscles of the intestine present a coherent layer; they are either exclusively (*holothurian*), or predominantly (large intestine), compressed into single band-like striae (*tæniæ*), between which the circular muscles are visible. If an electrical current leaves the muscle at any point of such a *tænia*, an obvious, localised, persistent contraction appears, which is absent when the current enters at the same spot; then, on the contrary, there is usually segmental constriction of the wall of the intestine, due to excitation of the circular muscles. If the anode happens to fall on any part of the surface of a saccule, the last-named consequences of excitation occur only the more plainly. If, on the contrary, the current leaves by the surface of a saccule, a small, scar-like swelling will appear (running at right angles with the direction of the fibres), which remains localised to the immediate proximity of the kathode, and—as may be recognised with artificial enlargement—is essentially caused by a local persistent contraction of the circular muscle-fibres only. This appearance is throughout analogous with the small, sharply-defined transverse swelling of *Holothurian* circular muscles apparent on kathodic excitation. This local kathodic excitation of the circular muscles of the intestine is less visible, for obvious reasons, in all cases where a longitudinal muscular layer of considerable thickness is present. Yet the peculiar dented constriction of the upper surface of the small intestine, from the centre of which the scar-like swelling arises, must be referred partly to the local kathodic excitation of the circular muscles covered by the longitudinal fibres. So too, the tendinous origin of a *tænia* of the large intestine appears with kathodic excitation to be concerned in the production of a local circular muscle swelling. If the peculiar and characteristic reaction of the circular muscles of *Holothuria* on anodic excitation, as well as the corresponding excitation effects in the muscular integument of worms, is remembered, there can hardly be a doubt that the circular, or segmental, constriction of the intestinal wall at the anode is due to the same causes. The relations are not indeed as clear and easily recognised as in the former case, and least so in the small intestine. The well-filled colon of *Herbivores* seems much more appropriate to these manifestations. Here, with weak

currents, the contraction at the anode is not total, and under certain conditions, particularly when the surface of the intestine has become dry, it is evident that the immediate proximity of the anode remains smooth at closure of the circuit, while in consequence of the contraction of the circular muscles, innumerable wrinkles are formed on both sides of it. Nor are the longitudinal muscle bundles of the *tæniæ* unexcited if the anode is placed anywhere along their course, only the effects are more easily overlooked in this case. The immediate proximity of the anode is again unexcited, while contraction occurs in the neighbouring region. In the thin intestine, where the anatomical relations are still more unfavourable to electrical excitation than in the muscular integument of worms, the corresponding manifestations of excitation, as described, are very difficult to analyse in detail, and only the marked and extended closure contraction of the circular muscles remains as a visible effect at the anode, along with the local shortening of the longitudinal fibres at the kathode. It cannot, however, be doubted that in the first case the longitudinal muscles, in the second (at least with strong currents) the circular muscles, also, are excited simultaneously, and to the same degree (29).

With the last-described experiments on the intestine of warm-blooded animals, must naturally be classed the results of Engelmann's extensive experimental investigation on the electrical excitation of the ureter (5). It is obvious, in view of the inferior size of this tube, which consists of circular and longitudinal muscles arranged similarly to the intestine, that the finer details of changes of form in the two muscular layers at the poles of the exciting current are here much harder to recognise than in the previous cases. For this reason, an effect which only appears exceptionally in the intestine, comes prominently forward in the ureter, *i.e.* the peristaltic progress of excitation, or contraction, from its starting-point. Schillbach (32) states, that on exciting the intestine with the constant current, "a contraction localised to the seat of excitation formed itself at the kathode," while at the anode a local contraction appeared, which in a few seconds was transformed into a marked peristaltic contraction upwards and downwards. We have frequently, in excised and still living (warmed) pieces of intestine, observed the peristaltic or anti-peristaltic progress of the contraction of the circular

muscles discharged at the anode. But just as the propagation of a localised excitation in the muscle of the intestine depends upon different, and so far not exactly determined, data, so too with polar effects of excitation. On the one hand, a high excitability of the excitable parts is apparently essential, while on the other, the nervous mechanism of the intestine itself seems again to play a very important part in the bringing about of progressive contraction. Most authors incline to the view that both the normal and the artificially excited peristalsis are caused solely and invariably by the intestinal nervous system (Nothnagel, Lüderitz, 33). Without taking a definite position in this question, which was discussed above, the possibility of propagating the excitation effects discharged at the poles of the constant current may be suggested. With the application of strong currents Lüderitz observed this at the positive as well as at the negative pole; but the kathode seemed to produce a stronger effect than the anode. "In the rabbit and guinea-pig this effect appeared in well-marked cases as a contraction of the longitudinal muscle of the intestine, extending for several cms., upwards and downwards, from the electrode, accompanied by a contraction of the circular muscles running exclusively, or chiefly, in the direction of the pylorus; in the cat the contraction of the circular muscles may run upwards and downwards, or in the direction of the pylorus" (33, p. 14).

In contrast with these uncertain, and still unexplained, data, the effects of electrical excitation of the ureter are characterised as well by the certainty of their appearance as by their great regularity. The thorough investigations of Engelmann showed that—apart from the slowness of the reactions—there is complete conformity with regard to the polar manifestations of excitation, between the ureter and striated skeletal muscle, so that these observations give cogent support to the theory of the unlimited applicability of the law of polar excitation. It is, therefore, at first sight the more surprising that, so long as the ureter remains *in situ*, the effects of electrical excitation with the constant current are diametrically opposite to what might be expected from Engelmann's investigations. On applying unpolarisable electrodes to two points along the rabbit's ureter, after exposing it with the utmost care and avoidance of unnecessary cooling, Engelmann found with closure of the

battery current that the muscular tube contracted at the spot in contact with the kathode, after a shorter or longer, but always directly perceptible, latent period, while the whole intrapolar area, as well as the anode, remained quiescent at the same time. Immediately after, a wave of contraction (similar to that which follows on localised mechanical excitation) starts from the kathode, in both the peristaltic and the anti-peristaltic direction. Just as the make excitation starts from the kathode, Engelmann found that the break excitation proceeds exclusively from the anode: the contraction always begins exactly at the point where current had previously entered the ureter through the electrode, never at the same moment in any larger area of the tract traversed. Here, as in striated muscle, the opening of the constant current is usually a weaker stimulus than its closure, so that greater intensity of current, and longer closure in particular, is required to produce any visible consequences. According to Engelmann, induced currents work exactly like constant currents of very short duration (current impacts), *i.e.*, as a rule, they only act as make stimuli, in which excitation proceeds from the kathode. It is only with very high excitability, and currents of great strength, that the contraction appears under certain conditions to begin at both poles simultaneously.

If in the guinea-pig, or rabbit, the two electrodes are applied, after removing the viscera, to different points of the ureter *in situ*, or if one electrode only is brought into contact with any given point, the other being applied to some indifferent part of the body, the excitation at closure will invariably proceed from the anode. Under such conditions there is never kathodic closure, or anodic opening, excitation.

With both the weakest and strongest possible currents, and, as a rule, independently of the position of the electrodes, and the direction of the current, the ureter is always constricted first at the anode, on closing the circuit, after which the wave progresses in both directions as described by Engelmann. The same applies to the break excitation, which after prolonged closure, with sufficiently strong currents, appears at the kathode. The nature of the contraction leaves no doubt that there is in both cases simultaneous excitation of the circular and longitudinal muscles. The smallness of the object makes it difficult to decide with certainty whether the closure contraction really proceeds

from the point of contact of the anode with the ureter, and whether, on the other hand, there is local continuous contraction at the kathode. The latter may indeed be ascertained by means of the magnifying lens, so that it can hardly be doubted that the polar excitation effects in the ureter *in situ* are manifestations analogous with the corresponding effects of excitation in the intestine.

The striking opposition between Engelmann's data, and the results of experiments on the organ *in situ*, suggests that the apparent reversal of polar effects depends essentially upon differences in the physical conditions, and in particular on the distribution of current. Experiments directed to this end have confirmed the correctness of the assumption, and may also furnish the key to the explanation of the manifestations which appear in many other smooth muscular parts in the proximity of the anode, and which we have previously referred to. Since the excised ureter of mammals is still excitable after several hours, if warmed to body-temperature, it is easy to experiment on it under different conditions. If such a preparation is laid upon a glass plate, warmed from below at 38–40°, and wetted with physiological salt solution, or better, with a small strip of moist filter-paper, the consequences of excitation, when the electrodes are applied anywhere along the muscle, coincide in respect of localisation with Engelmann's results from the ureter of the living animal. It appears as clearly as can be desired, however the electrodes are applied, that the ureter lying loosely upon its attachment constricts at the kathode at the moment of closure, after which the contraction progresses in undulations, or in one or the other direction. The same occurs at the anode with stronger currents, and longer duration of closure, on opening the circuit. If the excised ureter is then, without otherwise altering the conditions of experiment, laid upon a thick pad made of layers of filter-paper, or on a sufficiently heated block of salt clay, an opposite reaction will be exhibited with equal regularity, with both bipolar and unipolar excitation, since, as in the fresh organ *in situ*, the make excitation appears at the anode, the break excitation at the kathode. It is clear that this can only be explained by differences in current-distribution. If the thin muscular canal of the ureter is stretched freely, or on a non-conducting support, the current will be distributed somewhat according to Fig. 91 (after Engelmann).

It is evident that if the make excitation occurs only at the point where current leaves the muscular integument (the latter is hatched in the figure) the same could, and indeed must, be the case in the proximity of the positive electrode also. "If the branches of current drawn in the figure as proceeding from $E+$ (the anode) are followed, it will be noticed that a part of them leave the muscle-substance at the points $c' c'' c'''$. These points (secondary kathodic points) lie in the immediate proximity of the positive electrode, but are of course, with regard to the muscle-substance, to be viewed as the negative pole (physiological kathode). And here the closure excitation makes its appearance." That this does not actually occur, is referred by Engelmann in part to the differences in current density on the side turned towards, and away from, the electrode, in part to the depression of excitability and conductivity of the contractile substance in the region of the

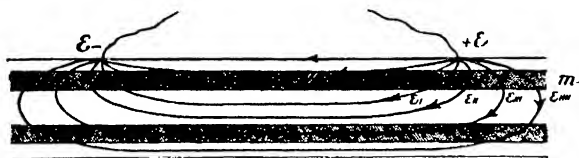


FIG. 91.

positive electrode (*infra*). A much wider distribution of the lines of current, and hence a richer development of secondary kathodic points in the region of the anode, and conversely of secondary anodic points in the region of the kathode, occurs, however, invariably whenever the ureter is left *in situ*, or placed on a moderately good conductor (Fig. 92). Conditions being favourable, excitation (contraction) will then occur on closure of the current at innumerable places in the proximity of the anode (not at the anode itself), and is either transmitted as an undulation (ureter), or remains localised as a persistent contraction. Conversely, further diffusion of the closure—excitation discharged at the kathode proper is hindered by the vicinity of secondary anodic points.

It can hardly be necessary to point out that these considerations are legitimate and valid in all the cases previously quoted, where, as in the muscles of *Holothuria* and *Echinidae*, and also the muscular integument of worms, and the intestine of verte-

brates, the conditions required for a wider distribution of lines of current in the proximity of the electrodes, and therewith also for the effectuation of secondary electrodes, are *a priori* and unavoidably present. The conspicuous thickness of all these parts is the reason that the lines of current do not, even with bipolar excitation, adjust themselves (as in the exposed nerve, or ureter) mainly in a direction parallel with the long axis of the organ, between the two points in contact with the electrodes, but that there is inevitably a further distribution, and, so to speak, diffusion, of the current in the proximity of the point where it enters, as well as that where it leaves, the muscle. The most important result of these experiments, in various parts of smooth muscular organs, is undoubtedly

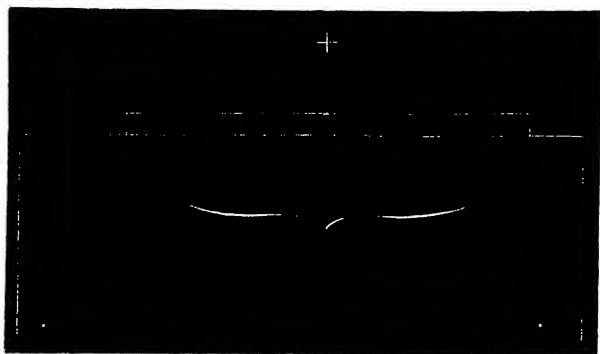


FIG. 92.

the fact that *in conformity with the law of polar excitation, as established for striated muscle, the make excitation is without exception discharged at the physiological kathode only, i.e. the true point of exit of current from the contractile substance of the entire muscle, and is seldom transmitted beyond this point; while, on the other hand, excitation never appears at the physiological anode itself on closure of the circuit, but where a state of tonic contraction is present, local inhibition of the existing excitability may appear as a more or less obvious localised relaxation of the muscular tissue, followed occasionally, when the current is opened, by a contraction which in extension and character exactly resembles the persistent cathodic closure contraction. While this last nearly always appears as a tolerably well-defined swelling, a persistent closure contraction of quite a different character may often be seen on both sides of the*

ELECTRICAL EXCITATION OF MUSCLE

anode, extending over a large area; in individual cases (intestine, muscular integument of worms, ureter) this gives the impression that the make excitation proceeds entirely and chiefly from the anode, a view that has already been expressed by Joffé with regard to the intestine (34).

It may be questioned if there is any analogue to this reaction in striated skeletal muscle. But before entering on this discussion, it will be advisable to go a little more closely into the allied, and from various points of view highly interesting, phenomena in cardiac muscle (35). Since the heart alternates rhythmically between contraction and relaxation, we are able to test the action of the current in both phases. It is advisable to use the heart of a cold-blooded animal, beating as slowly as possible—*e.g.* a large and well-cooled frog. If two fine brush electrodes are then applied to the surface of the ventricle at two parts as wide apart as possible, with persistent closure of a sufficiently strong battery current, a very striking result will ensue. At each new systolic contraction a local relaxation of the ventricle appears at the *anode* during closure of the current, in the form of a dark-red, blistered swelling; while on opening the current, on the other hand, the *kathodic* area is invariably first to relax during one or several systoles, presenting an appearance exactly similar to the anode during closure. These manifestations can be still better investigated with the unipolar method of excitation, one unpolarisable brush electrode being placed on any indifferent point, *e.g.* the skin of the throat, while the other, a finely pointed contact, is applied to the ventricle, in such a way that the circuit is never interrupted while the heart is in motion, without undue pressure. The effects vary according to the strength and direction of the current, and the condition of the heart-muscle at the moment of excitation. If the current enters by the electrode in contact with the ventricle, and closure is effected at the beginning of the systole, the first result of weak excitation (1 Dan., rheochord resistance 20, or more) will regularly be relaxation at the point of contact and its immediate proximity, repeated at each new systolic contraction as long as closure of the current continues. With increasing intensity of current there is a corresponding increase in the degree and amplitude of the relaxation, which at first is strictly local, standing out from the pale, contracted, surrounding area as a little red speck, scarcely 1 mm. in

diameter. This grows more and more prominent as a congested expansion of the muscular wall of the ventricle, spreading with comparative rapidity on all sides beyond the region of primary relaxation. As Schiff correctly observes, with reference to the analogous effect of local, mechanical excitation, the diastolic relaxation, after attaining a certain amplitude, sometimes appears to stand still for "a brief period," and then spreads slowly over the whole ventricle.

In other cases, however, we have observed as unmistakably, particularly in much cooled, slowly-beating hearts (which are used by preference in all these experiments), that the diastolic wave spreads with uniform rapidity from the seat of initial relaxation at the anode over the entire ventricle. Exactly the same effects as appear in the contracted ventricle at the anode, on closure of a constant current, occur unmistakably at the kathode immediately after the circuit is opened.

If with the same experimental conditions the current is reversed without moving the electrodes, it will be seen at break—given adequate intensity and duration of current—that at the moment of most pronounced systolic contraction the previously anodic, but now kathodic, part of the ventricle is always the first to relax itself. The diffusion of the originally local diastole increases again with the strength of current, but a second and no less important factor here comes into play, *i.e.* the duration of closure of the existing current. Up to a certain point a longer period of closure of a weak current can be substituted for the action of stronger currents. Stronger currents, however, are always required *a priori* to produce the kathodic opening as plainly as the anodic closure relaxation. The polar phenomena of relaxation thus described in the ventricle of the frog's heart contracted in systole may be very elegantly demonstrated, if the two finely-pointed thread, or brush, electrodes are placed at two points on the upper surface of the ventricle as far apart as possible in the longitudinal or transverse direction, with tolerably prolonged closure of a not too weak current. During the period of closure a local diastole occurs at the anode with each new systolic contraction. At break of the current the relations are inverted, and for two, or even several, successive systoles the kathodic region is the first to relax.

If it were possible to keep the frog's heart for long in con-

tinuous systolic contraction, the sole visible effects of electrical excitation with the constant current would be local relaxation of the muscular wall of the ventricle, appearing with closure at the anode, but with opening at the kathode—thus, as it were, forming an antithesis to the response of the muscle relaxed in diastole. It is difficult, and more or less incidental, to obtain a prolonged systolic contraction in the frog's heart; but, on the other hand, this is easily produced in the cardiac muscle of many invertebrates, *e.g.* snail's heart (35). We have already seen that a ventricle tied to a canula will often, if the latter is suddenly filled with fluid (snail's blood, 0.6 % NaCl), fall, after a longer or shorter series of regular contractions, into a state of protracted, uniform contraction. If during this time a current of 1–2 Dan. is led through it by means of unpolarisable electrodes, by allowing the suitably-moistened thread of the lower ligature of the apex of the heart to dip into a vessel with salt solution, in which one of the electrodes is already plunged, while the other pointed brush electrode is placed above the second ligature at the boundary between auricle and ventricle, an immediate relaxation of the ventricle may be seen in every case with closure of the circuit, which however—it must be noted—never occurs simultaneously at all points of the area traversed, but begins without exception at the end where current enters, *i.e.* at the anode. The relaxation always progresses in the direction of the current from the positive to the negative pole, and forms a more or less rapidly-transmitted wave, always, however, visible to the eye. If the current is only kept closed until the "wave of relaxation" has reached the kathodic end of the preparation, and is then broken, the ventricle returns as a rule—at least in all cases where the tonus was *ab initio* strongly developed—to its original state of continuous contraction. It is only in cases where a less pronounced tonus prevails from the beginning of the experiment, or where the preparation is excited at a time when the pulsations have begun again spontaneously, that an unbroken series of regular, rhythmical contractions follow a single short closure of the constant current, in which case they either persist indefinitely or give way after a time to secondary tonic contraction. In many cases the ventricle remains for several seconds, during the closure of the current, in a state of diastolic relaxation, after which only it begins the rhythmical peristaltic contractions. The anodic relaxation frequently

occurs more readily at one than at the other end of the preparation, and as a rule the base of the ventricle appears most favourable in this respect. This is probably related to the fact stated above, that the mechanical stimulus of the ligature often produces a pronounced local contraction at the apex of the heart, which, as was also pointed out, opposes much greater resistance to the action of the anode than the tonic contraction produced by the state of wall-tension.

If the electrodes are placed at opposite ends of the transverse axis of the ventricle, relaxation will begin, on closing the current, at the side of the anode, and accordingly the heart bulges out on the same side.

The intensity of current at which these phenomena appear is essentially dependent upon the strength of the existing "tonus." We have frequently obtained marked effects on using a Daniell cell, with rheochord resistance from a wire of 5 cm., and it may be taken as a general rule that with experimental conditions as described above, anodic relaxation rarely fails with a resistance of 100 cm. wire. If only minimal currents are employed, the relaxation is always confined to the close proximity of the point where the current enters. It appears at closure, and gradually disappears, even if the exciting current remains closed. In other cases it spreads, according to the direction of the current, over one or the other half of the ventricle. With moderate currents, and great excitability of the preparation, the propagation of the anodic wave over the *entire* ventricle is independent of whether the current is broken immediately after the effect appears, or whether it remains closed for a longer period. In the last case, however, the rhythmical contractions continue during the whole period of closure, and it should be noted that with each new diastole, relaxation invariably begins at the anode, and progresses from that point peristaltically. Hence, by merely watching the pulsations of a snail's heart, under the influence of the constant current, the direction of the current may be accurately determined.

The systolic contraction of the ventricle follows so much more rapidly that mere inspection will not suffice to determine whether under these conditions it also proceeds peristaltically (starting from the kathode), or not.

As previously stated, the rate of propagation of the anodic

wave of relaxation is so slow that its progress may conveniently be followed with the eye. For the rest it varies considerably. While in one case the wave requires several seconds to spread over the small tract implicated, averaging 5 to 7 mm., in other cases a fraction of a second will be sufficient. This, again, depends essentially upon the degree of tonus present, and one might say that the more pronounced this is, the slower will be the diffusion of relaxation from its starting-point. If the excitation is repeated with unchanged direction of current, or if the current is left closed, it is easy to see that the rate of propagation of the anodic wave increases in time up to a certain value—which it soon reaches; if the current is reversed it diminishes again quickly.

The period of latent excitation, generally speaking, varies in the same sense. The relaxation at the anode, as is immediately evident, never begins precisely at the moment of closure of the current, but is always preceptibly, often considerably, later, so that a latent period of one or more seconds is by no means rare. In many cases it may be shorter, but is never so brief that it cannot be detected directly by the eye.

If the experiment is made with preparations, which *ab initio* exhibit a marked degree of tonic contraction, the relaxation starting from the anode appears to be the sole *visible* effect of the current, a previous increase of contraction under such circumstances being at all events imperceptible. That such increase is, however, present under certain conditions of relaxation, may be ascertained in all cases in which there is primarily only a medium degree of tonic contraction. For then, with closure of an adequate current, the ventricle may be seen to contract in the first place simultaneously, in all its parts, after which only the peristaltic relaxation from the anode commences.

If the contraction in this case proceeds from the kathode, as may be affirmed on the strength of experiments to be described later, the conclusion which appears from the reaction is that the latent period of the kathodic closure excitation is smaller, while the rapidity of transmission is more rapid, than in anodic closure. On the other hand, the latter seems to take effect at a lower intensity of current, *e.g.* we have repeatedly found, with a weak tonus, that a (local) relaxation began earlier, *i.e.* with less rheochord resistance, than in the closure contraction in question.

Engelmann showed that every little muscle-bridge which unites two otherwise separate parts of the frog's ventricle, effects a physiological process of conductivity between them, inasmuch as the excitation coming from the auricle is carried through the bridges to the lower portion of the ventricle. There is thus a conductivity of excitation from cell to cell without any interposition of nervous elements. Similarly it may be shown that the anodic wave of relaxation is propagated from one half of the ventricle to the other, if any minute portion of the normal muscular wall remains to establish connection. By carefully pinching the side of an anodically relaxed ventricle of a large snail's heart with small forceps, it is easy to make the greater part of its wall in the middle section incapable of conducting. When subsequently traversed by current, relaxation can be seen to pass over the small conducting bridges, although far more slowly than under normal conditions.

A contusion extending right over the middle part of the ventricle, and dividing it into two excitable halves separated by a small, unexcitable zone, affords a means of investigating the phenomena which appear on excitation with the constant current more exactly than is possible in the entire uninjured heart. The experiment, indeed, presents certain difficulties, since, owing to the great sensibility of the preparation to mechanical excitation, the two halves of the ventricle are not seldom unequal in their capacity for response, one or other of them remaining more distinctly contracted, or, at all events, not returning to the relaxed state; but notwithstanding this, a little practice will generally obtain the desired result—provided the animals are large enough. If such a preparation is traversed by a battery current of sufficient strength, we see—as is to be expected—that only the anodic half relaxes, while the kathodic either exhibits no changes, or contracts distinctly on closure of the current if its tonus is but little apparent. On opening the circuit this reaction is exactly reversed in favourable instances; the kathodic section of the ventricle relaxes, while the anodic goes into contraction. It should be noted that both halves of the ventricle have their physiological anode and kathode. That, notwithstanding this, an effect can be detected upon one side only, is necessarily due to the fact that the density of current is less, on the one hand, at the point of injury (owing to the larger section), while, on the

other, there is injury to the muscle-substance, caused by mechanical impact.

Especially remarkable in this method of experiment is the relaxation immediately consequent on break of current at the effective kathode; it can in no respect be distinguished from the anodic closure relaxation, and, as we shall see, must in all probability be regarded as an equivalent process.

With regard to time, the order of succession of these phenomena is that the kathodic half contracts immediately upon closure, after which the anode begins to relax. Similarly, on opening the anodic break excitation, characterised by a strong rapid contraction of the section of ventricle affected, the kathodic opening effect follows, and—like the anodic make—produces relaxation of the previously contracted parts. There is thus a coincidence between the effects of the kathodic make and anodic break excitation on the one hand, and the anodic make and kathodic break on the other.

It is important to the significance of the kathodic opening relaxation to observe it at its best upon fresh, excitable preparations, and in a few successive makes or breaks only. The effect grows weaker and more obscure in proportion with the length of closure, or frequency of stimulation, with uniform direction and strength of current, and finally it fails altogether. Whatever means of excitation may be employed, we have observed this to be especially conspicuous in certain cases where, after double ligaturing of the apex of the heart, resulting in pronounced contraction, the effect occurred on one side only with subsequent passage of current. The entire descending current of a Daniell cell produced in this case a marked (anodic) relaxation at the base of the otherwise uninjured ventricle, extending only over a very small portion of it. Closure of the ascending current produced no effect, or at most resulted in a weak contraction of the previously relaxed upper section, while, on the other hand, after a prolonged closure of about 4 secs., the kathodic opening relaxation appeared at the base with great distinctness, though only in a few consecutive excitations. Having once become aware of this effect, we repeatedly obtained the same result on the normal heart immediately after attaching the canula, when the tonic contraction had developed itself. Two conditions are here essential: first, the preparation

must be fresh, and as excitable as possible; second, the current must not be too weak, nor closed for too brief a period. As a rule, 2 to 3 secs. closure was sufficient with the full strength of a Daniell cell. After the first anodic wave of relaxation has run out, the ventricle contracts in systole, next a peristaltic diastole sets in, and so forth. If the current is broken shortly after the second or third systole has begun, a diastolic wave, beginning at the kathode, may frequently be seen to sweep over the entire ventricle, *i.e.* diametrically opposite to the former direction. Sometimes this may still be detected in the second and even third diastole after the current has been opened, followed at the point of peristaltic relaxation, if the pulsations continue, by a diastole which seems to commence simultaneously all over the ventricle. From this we may infer that the kathodic break, like the anodic make, relaxation, propagates itself from cell to cell (by conductivity) from its starting-point. This conclusion, together with the fact that the first-named effect only occurs plainly under the most favourable conditions, seems to exclude the hypothesis that it is a manifestation of fatigue, produced by persistent kathodic excitation. It is much more probable that we are here in face of a characteristic and active reaction (equivalent to the anodic closure effect) of tonically contracted cardiac muscle.

These facts relating to the effect of the electrical current upon the cardiac muscle of invertebrate and vertebrate animals may no less appropriately arrest our attention than the excitation effects previously described in smooth muscle, since they form a distinct contribution to our knowledge of the effects of the electrical current. We see, in the first place, that the kathodic make and anodic break contraction are by no means the only visible effects of electrical excitation, but that an antagonistic *inhibitory effect* also occurs occasionally during an existing state of excitation, and expresses itself as the relaxation of a previously contracted part. Since, in the great majority of cases relating to the electrical excitation of contractile structures, the latter are in a state of comparative quiescence at the moment of excitation, it is intelligible that nearly all observations should refer to those manifestations of activity which it has alone been usual to regard as excitation phenomena. But the investigation of appropriate objects further shows that the

electrical current, of which the direct and normal effect is contraction of the relaxed and "resting" muscle, is able no less legitimately to *inhibit* a pre-existing excitation, and to produce an active relaxation of the contracted muscle. It may further be demonstrated that these "inhibitory effects" of the current cause true "polar effects" just as much as the excitatory process, and as in this last two "excitations," distinct with regard to time and place, if otherwise equivalent, may be distinguished as the closing and opening excitation, so here it seems justifiable in the cases cited to speak of two equally distinct "inhibitions," a closing and an opening inhibition, or, more properly, anodic and cathodic inhibition, inasmuch as the one appears at the point of entrance, the other at the point of exit of the current. It was to be expected *a priori* from the complete coincidence in physiological properties between cardiac and skeletal muscle-fibres, that under favourable conditions there should be polar effects of inhibition at the latter also.

It is evident that, in order to decide this question, a suitable muscle must be thrown into a state of persistent excitation, comparable with that of cardiac muscle during systolic contraction, or during the characteristic "tonus" of the snail's heart. This is best effected by the use of veratrin, which, as has been said, so changes the muscle-substance that after a short impact of stimulation there is not, as under normal conditions, a rapid *twitch*, but a prolonged tonic contraction, often persisting unchanged for several seconds, during which period the effects of the electrical current can be conveniently studied (36). We have found it advisable to introduce 6 to 7 drops of acetate of veratrin (1 % solution) into the posterior lymph-sac of a frog, which was killed about ten minutes later. The typical curve of contraction of a muscle thus poisoned (sartorius) has already been described. It is only necessary to recall the effect observed when a muscle, fixed in the middle, and extended in Hering's double myograph, and excited by a single induction shock, is traversed, after the maximum of contraction has been reached, by a battery current, preferably ascending. The anodic half of the muscle will then, at the moment of closure, lengthen considerably, and the corresponding curve makes a sudden drop, while the cathodic half, as a rule, becomes more contracted at the same moment, or at any rate shows no longitudinal changes. If the current is then

opened after a short closure, diametrically opposed changes of form will be visible in favourable cases in both halves of the muscle. The anodic half shortens, often in no inconsiderable degree, which must obviously be the expression of the break excitation, while at the same time the kathodic half is more plainly relaxed than would presumably have been the case without the intervention of excitation. On rapidly repeating the stimuli, with uniform direction of current, the same phenomena appear, though in diminishing quantity, as at the beginning of the excitation, for as long a period as the muscle remains in any

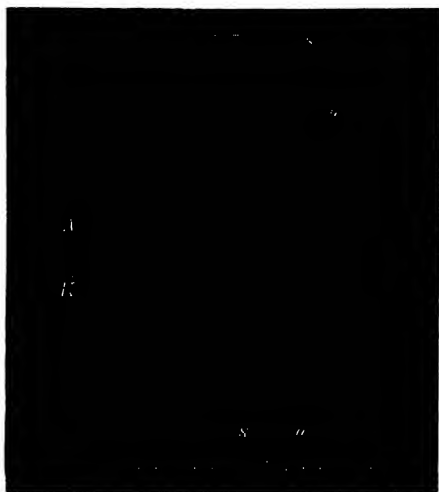


FIG. 93.—Sartorius fixed in the middle (double myograph). Persistent veratrin contraction. *S*, closure; *O*, opening of a constant current. Relaxation occurs at the anodic (*A*), contraction at the kathodic (*K*), half of the muscle.

considerable contraction (Fig. 93). From this it would seem that we are here concerned essentially with *local* changes in the muscle, confined to the immediate proximity of the physiological anode or kathode, and not, as in cardiac muscle, extending over a larger area. The changes of form described above in the sartorius, thrown by veratrin into an artificial state "analogous to tonus," present a complete analogy with the consequences of electrical excitation in systolically-contracted cardiac muscle, as above described. Here, too, along with the ordinary effects of polar excitation (which for the rest appear less

plainly than during the resting condition, and may even fail altogether), polar inhibitory effects may be directly demonstrated, and express themselves in the quelling, or diminution, of a previously existing state of excitation, and in a relaxation conditioned by the same, which is in the first place local. The well-known lengthening, at closure of a homodromous current, of the muscle in persistent opening contraction must be regarded as a kindred phenomenon, preserving a distinctive character only in so far as in this case there is inhibition of the state of excitation produced by the after-effects of the previous current at the physiological anode. Since a kathodic break inhibition may also be demonstrated, at least incipiently, upon the veratrinised muscle, where the curve in question drops suddenly, the hypothesis of two inhibitory processes, antagonistic to the polar excitatory processes (which do not, as a rule, find visible expression in striated skeletal muscle, while in many smooth muscles, as also in cardiac muscle, they are easily demonstrable during systolic contraction), would appear to be perfectly justified.

A few points still remain for consideration, *i.e.* certain phenomena which may appear at closure during the electrical excitation of striated muscle, and are obviously analogous to the excitation phenomena appearing at the anode in many smooth muscles. In both cases the effect is due solely to the appearance of secondary kathodic points. We have already seen that in the longitudinally traversed sartorius (fixed by the middle clamp) there is frequently, with strong ascending currents, a well-marked persistent closure contraction in the anodic half of the preparation also, which cannot be referred to an encroachment of the persistent K.C.C.¹ This is most plainly seen with injury (death) of the kathodic end. In this case even very strong, admortal currents (*i.e.* directed towards the demarcation surface) fail to produce any trace of continuous contraction at the limit of demarcation, although the muscle twitches sharply upon closure of the circuit; on the other hand, there is invariably a continuous contraction at the anodic end of the muscle, which increases directly with the strength of current. This

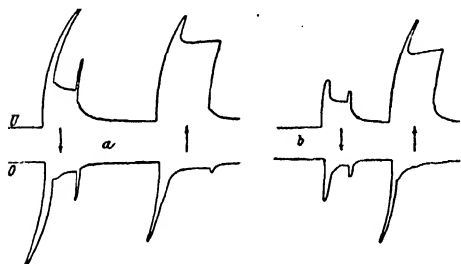
¹ A.C.C. = Anodic closure contraction.

A.O.C. = Anodic opening contraction.

K.C.C. = Kathodic closure contraction.

K.O.C. = Kathodic opening contraction.

effect is unmistakable to the unaided eye, or with a magnifying lens, but with the graphic method many additional details can be detected. If a sartorius (stretched in the double myograph, killed at the pelvic end, and clamped in the middle) is excited by currents of increasing strength (4–8 Dan., with rheochord), the first effect produced will be only the normal reaction of muscle injured at one end, as described already. Excitation with a descending current is followed by a pronounced make twitch (fairly symmetrical in both halves of the muscle), with a subsequent persistent contraction, which appears in the kathodic half only. The closure of the ascending current is at first without any effect, even at such a strength of current as would in the normal muscle provoke maximal closure contractions under the same conditions. Beyond a certain limit of intensity, however, the ascending (admortal) current once more begins to excite at closure, often indeed before an effective break excitation appears with the same direction of current under conditions favourable to its development, because the current is of greater density at its exit from the small end of the muscle.



Fr. 94.—Sartorius fixed at the middle, killed at the pelvic end (O). (8 Dan.) Persistent anodic closure contraction. After a pause of twelve minutes the effect of the ascending make excitation (at b) had decreased considerably, while the ascending excitation remained uniform.

The make excitation always expresses itself at first as a pronounced twitch on the anodic side without any conspicuous persistent contraction. With increased strength of current, however, this appears also, *exclusively in the anodic half of the muscle*; the kathodic

half relaxes completely after the make twitch has subsided (Fig. 94).

At a certain strength of current the latter nearly always overtops the twitch at closure of the descending ("abmortal") current. With increasing current intensity, the persistent A.C.C. increases rapidly at the lower end of the muscle, and in its turn soon exceeds the persistent K.C.C. of the descending current in magnitude and extension (Fig. 94).

In addition to this, the gradual swelling of the persistent

A.C.C. with repeated excitation is very noticeable. There is little doubt—as could easily be verified experimentally by time-measurements—that the closing twitch in a parallel-fibred muscle killed at one end is discharged with a sufficiently strong admortal current in the anodic half of the muscle, from whence it is propagated outwards. This appears, *inter alia*, from the fact that under these conditions the curve of the twitch on the anodic side is considerably larger than that at the kathode, while in all cases where excitation starts from the kathode alone, the corresponding half of the muscle is most strongly contracted.

Direct observation of the anodic end of the muscle, preferably with the magnifying lens after previous banding with sepia, shows that the persistent anodic contraction which appears with closure of strong currents, extends, unlike the well-marked persistent K.C.C., over a fairly large area, never, however, producing, as in that case, a swelling at the exterior ends of the fibres, which are, indeed, rather extended visibly, *i.e.* are unexcited. The two or three most internal bands of sepia, as well as the uncoloured spaces between them, do not perceptibly decrease or approximate (as is characteristic at the kathodic end), whereas, on the contrary, the more central bands do decrease and draw together, curving conversely towards the anode. This leads to a contraction swelling, starting from the continuity of the muscle, but close to the anodic end, and gradually dying out towards the middle. If one electrode (kathode) is applied to one of the two bone stumps of the sartorius, while the finely-pointed anode is in contact with any point of the surface of the moderately extended muscle, it is apparent, even with weak currents (2–3 Dan.), that there is no trace of contraction at the actual point of entrance, and with sepia marking it is easy to see that at such a point there is a not inconsiderable extension of fibres,—as appears plainly in a corresponding expansion of the cross-band in contact with the electrode, as well as in the adjacent segment of fibres. This passive extension at the entrance of the current is caused by a more or less pronounced contraction, which originates at both sides of the anode at closure, and persists during the passage of the current. By this method of experiment it is possible to observe the local anodic inhibition (relaxation) of the veratrin muscle more easily and plainly than with the above-described graphic method. It is only necessary to close the circuit twice

in succession without disturbing the electrodes: first, for a moment only, to produce sustained contraction of the veratrinised sartorius; and secondly, for longer, in order to observe the local relaxation at the anode.

If the normal muscle *in situ* is stimulated with unipolar excitation, the difference between kathodic and anodic effects is strongly marked, even with the weakest currents. While with punctiform contact of the muscle surface with the kathode, a local persistent contraction appears at the point of contact only, (after the make twitch has subsided), while the rest of the surface remains perfectly even, stimulation with the anode produces—in consequence of the persistent excitation in the bundles of fibres on either side of the point at which current enters—a deep, permanent, longitudinal furrow upon the surface of the muscle, while the actual point of contact and its immediate neighbourhood remains unexcited, and more or less extended, so that a flat, dented constriction appears.

With this mode of excitation the break effect shows very plainly as a small swelling, which appears at the point where the current enters, as soon as the circuit is broken, and remains visible for a long period. The similarity between this reaction in striated skeletal muscle, and the effects of electrical excitation in smooth muscle discussed above, is undeniable, so that the presumption of a fundamental uniformity in the response of these two kinds of muscle, as well as of cardiac muscle, to the electrical current, can hardly be disputed. This applies both to the manifestations of polar excitation, and the equally polar effects of inhibition. When it is remembered that the manifestations of excitation near the anode only appear with *weak* currents, on “unipolar” excitation, and, as found from recent experiments, fail altogether if the muscle (sartorius) dips into fluid, and is longitudinally traversed—appearing only at a high intensity of current, notably when the direction is ascending, if the preparation is stretched in Hering’s double myograph—it can hardly be doubted that we are again in face of excitation effects at secondary kathodic points, the existence of which, with unipolar excitation, is self-evident, but which must also be present, more particularly at the knee end of the sartorius, when current is sent in from the stumps of bone behind it. This is the necessary consequence of the peculiarly graduated

fibre-endings at this end of the muscle, which provide repeated opportunities for the current to escape into adjacent fibres of the muscle.

Although these phenomena are of no special physiological interest, they are deserving of thorough investigation, on account of the very striking polar effects—due to the same causes—in different smooth muscular organs, which might easily conduce to the fallacious assumption that there was a reversal of Pflüger's law of excitation. On the other hand, we find in them the key to a number of older observations on striated muscle. Even the earlier literature contains some—if rare—instances, which indicate that striated muscle, under certain conditions, if not invariably, exhibits a reaction to the electrical current which differs from the normal, inasmuch as at closure of the current, excitation appears on the anodic side also. The first observations in this connection are those of Aeby (20), dating from 1867, which led him, in opposition to Bezold and Engelmann, to the conception of a *bipolar*, though *unequal* excitation of the muscle, by the constant current. Moreover, Aeby thought he had proved that under certain conditions, more particularly with progressive fatigue of the preparation, the normal reaction—in which the excitatory action of the kathode far exceeds that of the anode—was exactly reversed. Aeby's experiments, however, are by no means unimpeachable, as both Engelmann and Hering (1) pointed out later. This applies in particular to an experiment in which the two legs of a frog still united by, and dependent from, the pelvis, are traversed by current, the two wires used as electrodes being connected to the lower end of the legs. The bones of the thigh were previously freed, and on excitation the leg traversed in a descending direction appeared to contract more markedly than that in which the current passed upwards, from which Aeby concluded that the effect at the negative pole predominated. But no account is taken, on the one hand of the difference between physical and physiological electrode points, as insisted on by Engelmann and Hering; on the other hand, of the difference in density of current at knee end and pelvic end of the two limbs respectively. Still, however, even in this case the reversal of effect becomes apparent after prolonged duration of experiment. Aeby concludes from this that fatigued and dying muscle possesses different properties from fresh muscle; it is no

longer excited to greater activity at the negative, but only at the positive, pole. Engelmann, also, came to the conclusion later that such a complete reversal of phenomena (*i.e.* of the law of polar excitation) might take place. But until it has been determined by unexceptional experiments, there must be great scepticism in regard to such statements.

Aeby also set up experiments in which a single muscle (*sartorius*, *adductor magnus*) was fixed at the middle with a clamp, so that both halves moved freely. By reversing the direction of current the twitch of one (the lower) half only was graphically recorded. "At the closing twitch more energy was invariably developed at the negative than at the positive pole, in a fresh muscle"; with very weak currents the kathodic half only contracted. The break twitch usually behaves conversely to the make twitch. Engelmann is inclined to refer this effect to the disturbance of conductivity at the clamped part, whence it would follow that, *e.g.* at closure, the excitation starting from the kathode cannot propagate itself without diminution to the anodic side. Here, again, however, Aeby's conclusion "that the negative twitch suffers much more from fatigue than the positive," and that with much fatigue the reaction of the fresh muscle may be inverted, appears to be of value. The preceding observations on the clamped *sartorius* might easily be recorded as a further confirmation of Aeby's conclusions (*cf.* Fig. 94), but the phenomena in question only appear characteristically with such strong currents that the effectuation of secondary kathodic, or anodic, points is not thereby excluded, and may, even in Aeby's experiments, have played a considerable part.

In conclusion, we must not omit the much talked-of alterations—hitherto investigated by the pathologist only—which appear after the peripheral paralysis of striated (warm-blooded) muscles, in regard to electrical reaction. These, as previously stated, express themselves partly in quantitative changes of excitability towards induced and constant currents, partly, as will be shown, by a qualitative alteration of the polar effects of excitation, and that in the direction stated above for Aeby's fatigued muscle. While, under normal conditions, the kathodic effect of excitation (so-called "kathodic closure twitch") preponderates considerably in direct unipolar excitation of a

muscle by the constant current, this ratio is reversed in paralysed muscles at a certain degree of degeneration ("*reaction of degeneration*"). Before giving a final judgment it would be necessary here, as in fatigued muscle, to make further investigations with unassailable methods, for the conditions under which alone the experiments in question can be tried in man, or have been tried on other animals, by no means correspond with the demands of an exact physiological method. On the other side, there are so many results, derived from irreproachable experiments upon different muscles and nerves, which are opposed to the theory of a reversal of polar effects, that any supposed exception must *a priori* encounter suspicion, and can only hope for recognition if the conditions of experiment and all accessories are perfectly simple and obvious.

Among the visible manifestations of excitation which appear in striated muscle, in consequence of the electrical current, must be reckoned the so-called *Porret's effect* or *galvanic muscle-wave*. Kühne (37), in 1860, first described this remarkable appearance. A muscle with parallel fibres, traversed by a strong current, falls into a characteristic wave-like, or flowing, movement, which spreads in the direction of the positive current, and remains localised to the intrapolar area. Kühne only alludes tentatively to a possible connection of this appearance with the Reuss-Porret phenomenon of electric transfusion, but, on the other hand, he expressly points out the "deep internal relation to what, with electrical excitation, is termed a twitch." Du Bois-Reymond (38) also recorded this wave as an excitation effect, the expression of localised contraction proceeding from anode to kathode. The whole appearance, indeed, recalls in a marked degree the fine waves and ripples which sometimes appear in the frog's sartorius with mechanical excitation also, and show directly that "the wave is a form of muscular motion, which can arise *without any excitation by current*." Undoubtedly, waves of contraction of very different heights may spread over the muscle; "at one moment they are enormously expanded, at the next so fine that to the naked eye they only appear as a delicate ripple; sometimes they run in the single bundles quite independently of one another, so that many swellings can be seen to spread simultaneously in different directions; sometimes a single swelling extends itself over a larger area of the muscle surface" (Hermann, 39, p. 603). The velocity

of the wave varies considerably, but is always insignificant. Hermann (*l.c.*) estimates it in fresh, freely-undulating preparations at 4 to 5 mm. per sec. We have already shown that tolerably strong currents are necessary in order to produce a clear effect. It is fundamental to the conception of the wave as an excitation phenomenon that it is *exclusively characteristic of striated living muscle*, and is non-existent in other moist tissues;¹ further, as Hermann showed (*l.c.*), an effect of fatigue and recovery of the muscle may be demonstrated, since the energy and rapidity of the wave diminish gradually, to increase again after a prolonged period of quiescence. Above all, however, it must be noted that, as in muscular excitation in general, *the temperature of the moment affects the galvanic wave in a most striking manner*. On sending current through fresh muscles (sartorius) in a warm oil bath, Hermann (*l.c.*) found that the effect appeared in extreme perfection, no idea of which could be formed from ordinary experiments. The diffusion, as well as the height and velocity of the wave, are enormously increased by higher temperature; on the other hand, the effect disappears entirely with even moderate cooling. The effect of *muscular tension* is further very conspicuous. The wave is always most marked with the ordinary medium degree of tension, and ceases to be visible with either very high, or completely absent, tension. When the significance of the degree of tension at any given moment to muscular excitation (as also to metabolism) in the entire muscle is remembered, this reaction can hardly be surprising.

It has already been shown that the direction of the wave is always from anode to kathode, but *the anode itself is not the starting-point of the waves of contraction*. If excitation is effected with a current of such intensity that the wave is just perceptible, it appears, as a rule, to be most marked in that tract of the muscle which, during closure, is thrown into persistent contraction. It frequently happens that the extreme ends of the fibres on the anodic side, as also the entire kathodic half of the muscle, show no trace of the wave, while the greater part of the anodic side is

¹ On applying strong currents Neumann (12) frequently observed a phenomenon in cardiac muscle (of frog) which appears to be analogous with the galvanic wave, inasmuch as peristaltic waves spread during closure in the direction of the current in such regular succession "that the heart seems to give faint, delicate pulsations."

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thrown into pronounced undulation. *Invariably, however, the wave begins in the immediate proximity* of the anodic end of the muscle, and spreads thence in marked currents over the entire muscle. This points to a very close relation between the above-described persistent anodic closure contraction and the "galvanic wave," and it can hardly be fallacious to regard both phenomena as two different symptoms of one and the same change in the muscle. In this connection it is to be noted that Hermann (*l.c.* p. 602) occasionally received the impression that on opening the circuit "a short ripple or wave proceeded towards the anode—*i.e.* in the opposite direction to the characteristic phenomenon." Death or chemical change at the end of the muscle produced as little effect upon the galvanic wave as upon the persistent anodic closure contraction. If this last is admitted to be a manifestation of excitation depending upon the effectuation of secondary electrode points in the continuity of the muscle traversed by the current, the galvanic wave can hardly be regarded as different. In view of these results, the theory supported mainly by Jendrassik (40) and Regeczy (41) that the galvanic wave is principally due to the changes of form and place which the canaliculi containing blood and lymph in the entire muscle (or any part of it which consists of several bundles) undergo in consequence of the endosmotic transference of fluid particles within them, caused by the constant current, must be regarded as sufficiently contradicted, especially as—since Hermann's researches—there can be no doubt as to the active co-operation of the living and excitable muscle-fibres. Hermann's explanation (*l.c.*) of the galvanic wave, on the other hand, presents no objections. He starts from the unquestionably correct assumption that with even the strictest longitudinal excitation of a muscle with parallel fibres, "the majority of fibres have not merely *one* anodic and *one* kathodic point, corresponding with the electrodes of the entire muscle, but a great number of points of entrance and exit, due to the oblique or transverse course of the lines of current to single points of the fibres, especially where the latter are accidentally crumpled together." Strong currents set up excitation at each of the secondary kathodic points, by which a contraction swelling is produced, that spreads slowly towards the kathode. "The origin and progress of the swelling makes new changes and new irregularities between the lines of

current and the fibres, and thus *new excitation* is occasioned. In this wise the marvellous wave can be accounted for." Special attention, however, must be given, on the one hand to the starting-point of the wave, and on the other to the difficulty already pointed out by Hermann, that the wave fails to appear just when, as it seems, all the conditions are most favourable to the production of secondary kathodes by curvature of the fibres, *i.e.* in *completely relaxed* muscle. If it is admitted, as Hermann states, that under certain conditions of zig-zag curvature in the muscle, the physiological effect of longitudinal passage of current may be equivalent to that of purely transverse current—since in the one case, as in the other, the anode and kathode of the same fibre are exactly opposite—it must also be remarked that the wave is conspicuously absent in many cases, where curvature of the fibres can hardly be detected in the extended muscle. In order to explain the slow propagation of the waves of contraction (in one direction only), Hermann assumes that there is injury to conductivity within the entire intrapolar area, in consequence of excitation by strong currents. This, however, seems questionable when we reflect that a perfectly similar wave may also be observed *independently of the passage of current* in quite fresh muscle, if it is excited in a given way (mechanically). It was shown above that the same muscle may transmit slow and fast waves of contraction, without any considerable underlying alteration in its condition. It is due far more to the quality of the stimulus.

It is very essential to the entire theory of these manifestations of excitation in the continuity of the muscle (as to which there is still much to be explained) that we should know whether the electrical current does not produce further change within the area of muscle traversed, in addition to the polar effects described, or whether—as has, so far, been tacitly accepted—this tract is only indirectly affected by the action set up at the most important physiological points of anode and kathode. Here there is of course no question of the temporary effectuation of secondary electrode points. Von Bezold (10), to whom we owe the first thorough investigation into the electrical excitation of denervated muscle, included this question in his experimental inquiries, and replied to it by saying that, so long as current traversed the muscle at constant strength, there were continuous

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physiological changes in the *entire area traversed*, by which, on the one hand, the excitability, and on the other, the conductivity, of the intrapolar tract were fundamentally affected. Since changes in the excitability, or conductivity, of any section of the muscle can only be inferred indirectly from corresponding changes in the magnitude of contraction, observed at the same spot with uniform excitation, the main point in the case before us is to apply uniform stimuli to any point of the intrapolar tract, before, during, and after the passage of current, and then to measure the height of twitch by graphic methods. It is obvious that only the electrical stimulus is applicable in this case, since it alone permits of exact graduation of the strength, and does no immediate injury beyond the spot excited. But the application of the electrical current as a test stimulus of the excitability of a tract of muscle already traversed by current, has to contend with considerable practical difficulties on account of the hardly avoidable interference of the two currents. If the battery current, the effect of which is to alter the excitability and conductivity of the tract of the muscle traversed, is termed the "polarising," while the induction current, on the other hand, used as the test stimulus, is called the "exciting," current, it is clear that if the electrodes of the latter are applied directly to the muscle traversed by the constant current, current must necessarily flow from the one circuit into the other in proportion with the resistance in both circuits. But if the polarising (constant) current is partly diverted into the circuit of the exciting (test) current, a physiological kathode will necessarily be formed at one of the exciting electrodes, thereby producing a continuous state of excitation, which, on its side, complicates the effects of the test stimulus, so that temporary changes in the height of the twitch produced by the test stimulus before and after closure of the polarising current, cannot well be referred to alteration of excitability in the parts in question, which would be *independent* of direct excitation by the polarising current. The following point must, moreover, be taken into consideration.

According to the law of polar excitation, stimulation takes place—following the direction of the current—now at one, and now at the other, end of the tract traversed, on closure of the test current, from which it necessarily follows, owing to the oblique direction of the lines of current (from the lateral

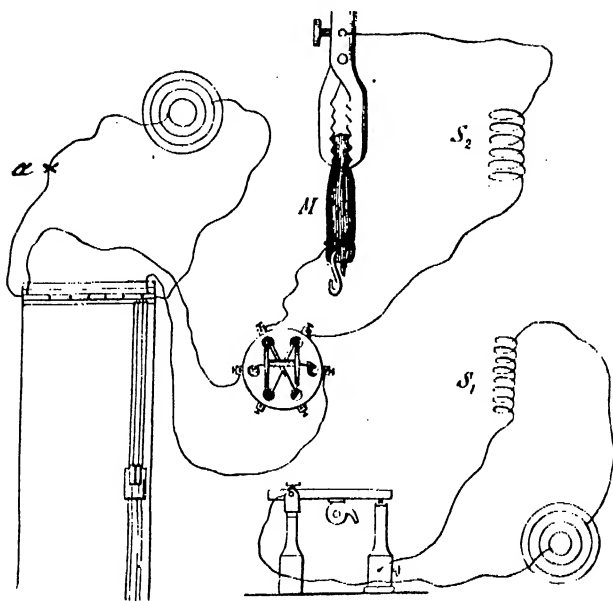
situation of the electrodes), that the physiological kathode, or anode, must possess a considerable extension. In the one case, therefore, if a branch of the polarising current diverges into the exciting circuit, the physiological kathode of the test current falls upon points of fibres that are already kathodic; at other times the contrary occurs, since the kathode of the test current then coincides with anodic points. The effect of the test current naturally depends upon its direction. Since the distribution of current into the two circuits depends solely upon the ratio of resistance, it is possible, in any given case, to throw such a resistance into the exciting circuit that the resistance of the short tract of muscle between the corresponding electrodes shall be minimal, to avoid a branching of the constant current into the exciting circuit (Hermann, *Handb.* II. i. p. 44). The experiment is arranged as follows: Two non-polarisable electrodes fastened to a movable holder, are applied in the usual manner to different points of a sartorius, stretched in Hering's double myograph. The make induction current is exclusively used as the test stimulus, and is led in by threads moistened with physiological NaCl solution, in order to interfere as little as possible with the changes of form in the muscle. The length of the intrapolar tract is about 3–4 mm., and its resistance is therefore negligible in comparison with that of a glass tube 2 m. long by 0.5 cm. in diameter, filled with very dilute CuSO_4 solution, introduced into the primary circuit. The twitches are recorded upon a smoked surface, one electrode of the double myograph being permanently fixed, while the other is in connection with a writing-point. The intensity of the polarising battery current is graduated as required by a rheochord. The closure and opening of the constant current is effected by a mercury key introduced between the rheochord and battery (2 Dan.). If the polarising and exciting current have the same direction (both descending), the case is, in the first place, conceivable in which the points of exit fall together, the negative test electrode being applied to the stump of the tibia, while the other is in contact with the end of the sartorius. In this case there will be marked alterations in the excitability (to be described below). Quite other results occur, when *both* exciting electrodes are placed in the continuity of the muscle. According to v. Bezold, it might be expected that during the closure of a very weak current, a

condition of increased excitability would spread from the cathodic end over a certain larger or smaller area of the tract lying between the poles. At first sight this seems to correspond with the observation that when *both* electrodes are so applied to the lower end of the muscle that one (kathode) is 2 to 3 mm. away from the tendon end, and the other about 4 mm. higher, the height of the minimal twitch discharged by the closure of a descending induction current, during polarisation by a very weak descending battery current, is greater than it was before. Closer examination, however, shows that this conclusion is not justified, the experimental result being due solely to the structure of the muscle. Since, *i.e.* the muscle-fibres are not all of the same length, and are inserted at the lower end into an oblique surface, the physiological kathode of the muscle traversed longitudinally in a downward direction, must necessarily extend over a measurable and tolerably extensive portion of the lower half of the muscle. So long therefore as, under the experimental conditions described above, a sufficient number of ends of fibres fall under the kathode of the test current, a perceptible alteration of excitation effects during polarisation—manifesting itself either as increase or as diminution of excitability—is perfectly intelligible. The latter, *i.e.* apparent extension or depression of excitability over the intrapolar muscle region may be observed under the same experimental conditions, either when with descending polarising and test currents the intensity of the former increases, or when with an ascending polarisation current the exciting electrodes, which are close together, are brought so near to the lower end of the muscle that the excitation is still in part discharged within the anodic area. If, however, the test electrodes are pushed farther and farther along the muscle to its upper end, it may easily be ascertained that with the given strength of the polarising battery current a perceptible change in the height of twitch before and during the passage of current cannot be demonstrated at any other point of the intrapolar area. It is therefore solely the spatial distribution of the points of entrance or exit of current at the lower end of the muscle, due to irregularities of structure in the sartorius, which occasionally produce a wider diffusion of the excitatory changes confined, as we shall see, to the physiological anode and kathode. If the negative test electrode lies outside the region of the physio-

logical kathode, or anode, of a parallel-fibred muscle traversed longitudinally, no changes of excitability will be displayed in the intrapolar area, in either a negative or positive sense, when polarising battery currents are applied of not excessive strength. Just as little would this be the case at break of the polarising current. It would thus appear that the electrical current may traverse the muscle without producing any directly demonstrable alteration of the substance with the sole exception of the polar points. Very different, as we have seen, is the reaction at the physiological kathode and anode proper. Here it is easy to demonstrate marked changes of excitability in a positive or negative direction, either resulting from a pre-existing persistent excitation, or as the after-effects of such, or caused by polar inhibitory processes. To this we must refer the observations of v. Bezold on alterations of excitability in the tract of muscle traversed, the method he employed being only adequate to test the excitability of kathodic and anodic points of fibres. Starting with the presumption that an induced current does not, like a constant current, act by *polar* excitation only, but that it excites all points of the area traversed simultaneously, and uniformly, v. Bezold endeavoured to test the so-called "total excitability" of the tract of muscle traversed by the polarising battery current, by making use of a break induction current as test stimulus, led into the muscle by the same electrodes as those which conveyed the polarising current. Von Bezold's experiments may be represented by the diagram (Fig. 95).

The secondary coil of an induction apparatus (S_2) is introduced into the battery circuit, the intensity of which can be regulated by a rheochord. If the constant current is opened at (a), an induction current will traverse the muscle in one or the other direction at closure or opening of the primary circuit, giving rise to a twitch in the muscle. If the battery circuit is closed at (a), a part of the current, at any given intensity as determined by the rheochord, will pass continuously through the muscle. If the primary circuit is again made or broken, an induced current of the same strength as before will traverse the now polarised muscle in the corresponding direction, the relations being obviously altered only in so far as the exciting current no longer starts from, and returns to, a density of zero, but from a density varying with the strength of the

polarising current. The second twitch, like the first, is recorded graphically, and thus we obtain a comparative tracing of the time-relations and magnitude of twitch in the muscle traversed (polarised), or not traversed, by current. If v. Bezold's presumption were correct, that all points of the tract through which current passes are excited simultaneously and uniformly, the comparison of the height of twitch in both cases would not indeed determine the changes of excitability in definite points of the intrapolar area, since the different elements would of



course participate collectively in such changes, each according to its particular state at the moment; but we should obtain the sum of resulting excitability, or as v. Bezold expresses it, the "total excitability," in the tract of muscle traversed. As, however, it has since been demonstrated that induced currents, like constant currents, have only polar action, the experiments described can, of course, show no more than alterations in excitability at the physiological kathode or anode. It is therefore evident that v. Bezold's method only determines the alterations in excitability at the ends of the fibres in a longitudinally

traversed muscle, and contributes nothing in regard to the excitability of the intrapolar region. Besides this principal fallacy, his experiments are also hampered by the use of metal electrodes, which complicate the results by polarisation.

In order to determine the *polar excitability* of a curarised muscle with parallel fibres, traversed by a constant current, from the above method—with as few fallacies as possible, and *during the passage of the current*—the uninjured sartorius, with its stumps of bone at either end, must be attached to the double myograph with unpolarisable electrodes, one of which is permanently fixed, while the other is movable, and connected with a writing lever. The arrangement is such that the polarising constant current and make induction current traverse the muscle *in the same* ascending or descending direction.

In order to obtain a general notion, and also for better comparison with the results of v. Bezold, we subjoin two out of many tables of results in which the same method is followed on the whole as in the analogous experiments of v. Bezold:—

I.

		Height of Twitch.
1. Twitch.	Muscle unpolarised	4 mm.
2. "	" "	4 "
3. "	Immediately after closure of very weak descending ¹ current (2 Dan. rheochord res. = 1)	29 "
4. "	Immediately after breaking this current	4 "
5. "	Muscle unpolarised	4 "
6. "	Immediately after closure of strong descending current (res. = 4)	32 "
7. "	On breaking this current	3 "
8. "	Polarising current strengthened (res. = 8) immediately after closure	26 "
9. "	3 secs. later	0 "
10. "	Immediately after opening the current	0 "
11. "	1 minute later	trace

II.

1. Twitch.	Muscle polarised	6 mm.
2. "	" "	6 "
3. "	Immediately after closure of weak descending current (2 Dan. res. = 1)	29 "

¹ Descending and ascending currents vary in effect because of the asymmetrical form of the sartorius.

						Height of Twitch.
4.	Twitch.	After 5 secs.	.	.	.	26 mm.
5.	"	" 7 secs. more	.	.	.	21 "
6.	"	" 4 "	.	.	.	18 "
7.	"	" 4 "	.	.	.	16 "
8.	"	" 4 "	.	.	.	14 "
9.	"	" 5 "	.	.	.	8 "
10.	"	" 5 "	.	.	.	5 "
11.	"	" 5 "	.	.	.	0 "
12.	"	" breaking the current	.	.	.	0 "
13.	"	" 40 secs.	.	.	.	0 "
14.	"	" 50 "	.	.	.	3 "
15.	"	" 62 "	.	.	.	5 "
16.	"	Immediately after closure of same polarising current	.	.	.	25 "
17.	"	5 secs. later	.	.	.	21 "
18.	"	5 "	.	.	.	17 "
19.	"	5 "	.	.	.	12 "
20.	"	5 "	.	.	.	4 "
21.	"	5 "	.	.	.	0 "

It is obvious from these tables that, as v. Bezold found, very weak constant currents actually increase the excitatory effect of single induction currents sent through the entire intrapolar area, provided they are in the same direction. The numbers quoted show, moreover, that the increase in height of twitch is much more significant than was formerly observed by v. Bezold. This is in great measure owing to the fact that the otherwise unavoidable and rapid decrease of intensity in the weak polarising current is prevented by the use of unpolarisable electrodes.

An essential difference, however, between these results and those of v. Bezold appears when the effect of *duration of current* upon the consequences of test excitation are taken into consideration. While, *i.e.* v. Bezold found on application of a polarising current that the height of the twitch discharged by an induction shock increased perceptibly with the duration of the constant current (notwithstanding the disadvantage of progressive polarisation from the metallic electrodes), we have never experienced this. Rather, when the battery current was at first of *very low* intensity, so that no visible sign of excitation appeared at the moment of its entrance into the muscle, the height of the augmented twitches discharged by a homodromous induction current, did not alter perceptibly, provided the polarising current was not closed for too long a period. On the other hand, a more or less pro-

nounced *decrease* in height of twitch could be observed in the latter case, under uniform conditions. It is, moreover, unmistakable that the excitability of the preparation just before polarisation commences, determines the time in which the diminution of excitability occurs after closure of the constant current. As a rule it may be said that depression follows the period of heightened response, in the kathodic fibre points of a weakly-polarised muscle, the more quickly in proportion as the excitability of the muscle is *ab initio* lowered from any cause, local or general.

This is exhibited as well in preparations taken from frogs with deficient vitality, as in those in which excitability is only locally diminished (at the kathode) by the temporary passage of current. The latter effect can also be seen in Table II. of the experimental series. Within 34 secs. after closure of the weak polarising current the augmentative effect of the homodromous make induction current used as test excitation—at first strongly marked—became practically zero. So soon after break of the constant current as the muscle had recovered itself sufficiently to yield distinct twitches with the same test as before the first passage of current, the polarising current was closed again. The height of twitch immediately reached the same proportions as in the first series; on the other hand, the excitability of the kathodic points of fibres diminished much more quickly than before, since a passage of current of 20 secs. suffices to inhibit the effect of the same stimulus. The depression and final inhibition of previously augmented excitation caused by a homodromous induction current, makes its appearance more or less quickly in proportion with the intensity of the battery current sent through the muscle.

Starting from minimal polarising currents, gradually increased in intensity by pushing up the rheochord slider, and giving the muscle time to recover itself between each pair of experiments, it is easy to verify the accuracy of this last statement. At a certain intensity of current, varying in proportion with the excitability of the preparation, the increase of kathodic response only occurs plainly at the moment immediately consequent on closure, and is hardly perceptible with further augmentation of current intensity. This does not, however, as might be concluded from the foregoing observations of Engelmann on the rabbit's ureter, occur for the first time when the constant current has

already produced an obvious, persistent K.C.C.; on the contrary, the stage of augmented response in most cases eludes observation (on account of its excessively short duration) if the intensity of the polarising current is insufficient to discharge a maximal closure twitch in the muscle. It is therefore a universal principle to employ only the weakest battery currents when the object is to demonstrate a marked increase of response in the kathodic points of the fibres at a given stage of polarisation, since it might otherwise be easily overlooked. Hermann (42), together with Pflüger and Nasse (in older experiments), finds that "in nerve, as well as in muscle, the effect of a given induction current is increased by homodromous constant currents, and depressed (to abolition) by opposite currents." Beginning with the weakest constant currents, the increase of excitation from homodromous variations of current gives way to diminution when the strength of the constant current exceeds a certain limit; Hermann obtained the same results in a still more unexceptional manner by using battery currents *for excitation*.

In Tables I. and II. (*supra*) the twitches discharged by the test stimulus immediately after closure of the battery current were approximately maximal. There is thus an *a priori* probability which receives experimental confirmation, that *the responsiveness of the kathodic points of fibres in a muscle traversed by current increases up to a certain limit with the intensity of the polarising current*. This limit, however, is very low; in our own experiments it was reached as a rule at 1-2 cm. deriving circuit, with 2 Dan. as the battery. Beyond this limit, excitability diminishes, as has been shown, in proportion with the strength of the polarising current.

It is just in the case in which the intensity of the latter is so low that each increase of it produces a corresponding augmentation of the excitatory effect of a homodromous induction current, that the increase in height of twitch corresponding to increased duration of closure of the battery current, recorded by v. Bezold, might be expected; but in no instance has it made its appearance.

What conclusions then may be drawn from these experiments? Since we know that the induction current used as test stimulus generally produces visible excitation at the kathode only, *i.e.* at points of fibres which, during the closure of the polarising current, are already in a state of persistent excitation, the con-

dition of excitability at the kathode, varying as it does with strength and duration of current, must be regarded solely as the consequence of localised persistent excitation, and the question is only how there comes to be sometimes an increase, and sometimes a depression, of excitability.

It must be admitted that the electrical current traversing a muscle acts as an exciting agent, not merely at, but during the whole period of closure. Further, it has been established experimentally, that the alterations in the contractile substance which underlie the excitatory process are confined to those points of fibres by which the current leaves the muscle. Each experiment shows, moreover, that the appearance of a make twitch, *i.e.* discharge of a wave of excitation, or contraction, at the point of stimulation, as a rule implies the condition that the oscillations of current from zero, or any finite value, should occur with a certain rapidity; and it should be added that the absolute intensity of the excitation current also must surpass a given limit, if visible manifestations of excitation are to be elicited. Supposing that a muscle is persistently traversed by a battery current of such low intensity that its presence is not betrayed by any trace of visible excitation, we are none the less justified in assuming that a "latent condition of excitation" is, as it were, present at all those points of fibres which collectively represent the "physiological kathode," during the passage of current: for that altered state of the contractile muscle-substance, which, by its rapid appearance at the point where current escapes, sets up a wave of contraction as soon as the intensity of the current exceeds a given minimal limit, and the continuance of which during the closure of stronger currents is expressed in the continuous closure contraction, must obviously exist on closure of the weakest currents also, albeit in a lesser degree.

Only a small *sudden increase*, greater or less according to circumstances, will then be required, in addition to the constant but inadequate stimulus, in order to produce a wave of excitation at the kathode. In other words, a rapid, positive variation of a very weak current flowing through the muscle may effect an excitation, even when the same variation, starting from zero at the abscissa, produces no effect, or only minimal excitation of the muscle. The *increased* excitation occasionally to be observed with an induction current, homodromous

with the polarising battery current, may therefore be explained as the summation of two intrinsically inadequate stimuli, and the increased response at the kathode appears to be not so much a peculiar effect of current introductory to the excitatory process as the actual result of that process. This theory is quite compatible with the contradictory behaviour of a muscle during, and immediately after, protracted weak polarisation, or with the application of stronger currents.

The *after-effects* observable in the last case were referred above to local "fatigue" of the kathodic points of fibres, induced by current. The facts before us show that almost immediately after closure of a medium current there is, according to the duration of closure, a progressive diminution, or even complete inhibition, of response to induction currents at the kathode. The direct dependence of the depression of excitability during the passage of the current upon its duration, with low polarisation intensity, makes it highly probable that in this case the excitatory process itself, or, more correctly speaking, the fatigue induced by the same at the seat of direct excitation, must be regarded as the cause of the decreased response at the kathode.

The protracted condition of weak excitation at the kathode *gradually* produces alterations in the contractile substance of the muscle, as expressed not merely during closure of the current, but also for some time after it has been broken, in a diminished excitability, which is usually explained as a fatigue effect. It must be asked, however, how the diminution of response at the kathode immediately after the closure of stronger currents is to be understood and explained. Here there can be no question of "fatigue" in the ordinary sense of the word, because no conspicuous after-effect outlasting the stimulus can, as a rule, be demonstrated, owing to the brief duration of closure.

That it is not wholly wanting is shown by the fact that in a series of twitches produced by closing the constant current at short intervals, its direction remaining unaltered, the height of each twitch is perceptibly lower than that which immediately precedes it; this insignificant after-effect of a single short closure would not, however, suffice to explain the continuously marked depression of excitability at and during closure of the same current. An induction current which produces maximal twitches in the muscle not traversed by the constant current is totally

ineffective during the passage of a battery current of medium intensity in the same direction, while it recovers its former efficiency in full as soon as the constant current is broken.

But it must not be forgotten that even the excised muscle possesses a large capacity of recovery, by which it is enabled to equalise the changes in its substance caused by the excitatory process the more quickly and completely in proportion as the stimulus acts for a shorter time, or the preparation is intrinsically more vigorous. Engelmann's experiments on the ureter show that not only excitability, but conductivity also, appear to be affected after each contraction, *i.e.* after a relatively short excitation, and only recover themselves during the subsequent pause; and that the more quickly in proportion with the original excitability of the preparation. The "refractory" period of contracting cardiac muscle should also be taken into consideration. It is, however, clear that if the capacity of recovery in striated muscle is greater, and exceeds that of smooth muscle, in the same proportion as its excitability, diminution of response at the kathode, due to the excitatory process, may have reached considerable proportions after the closure of a strong current, without any necessarily marked after-effect on opening the current, provided that closure lasts for a few seconds only. But it is never possible to exclude a temporary effect upon absolute current-density, of such a kind that with an existing current of a certain magnitude, a superposed positive variation will excite in a lesser degree than before, independent of the fatigue induced by the former. We may therefore assume, that not only the depression of excitability during and after persistent polarisation, but also the depression of response at the kathodic fibre-points of a muscle immediately after closure of a strong current, depend essentially upon a local "condition of fatigue," meaning by "fatigue" the total changes in the contractile substance of the muscle, produced at the seat of stimulation by the excitatory process, which, while they last, prevent, or at least hinder, the rise of a second excitation. We may therefore conclude as the result of all the preceding data, that *the alteration, positive or negative, of excitability at the kathode of a muscle traversed by current, depends essentially upon the state of latent continuous excitation, and its consequences, which vary with the strength of the polarising current.*

It is less easy to formulate conclusions as to the manifestations of excitability at the "physiological anode" of a muscle, during the passage of current. The attempts at solving this problem by the application of induction currents, *opposed in duration* to the polarising current, and traversing the whole intrapolar tract, have been too ambiguous to give any decisive results. Von Bezold, who made the same experiments, though from another standpoint, asserts (10) that "both ascending and descending galvanic currents flowing through the muscle, increase its excitability at first to ascending make induction currents, so long as these do not exceed a certain density, at and after which point the effect is diminutional." Moreover, "the turning-point of the curve of increase of excitability, in ratio with the density of the polarisation current as abscissa, appears earlier when the polarisation current is opposed to the exciting current, than when it is homodromous with it." When the induced current is in

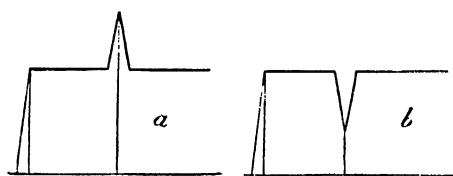


FIG. 96.

the same direction as the polarising current, the excitation of the muscle apparently ensues only because the constant current suffers a sudden, evanescent, positive variation at the moment of closure of the primary circuit¹ (Fig. 96, *a*).

The converse naturally occurs when the direction of the exciting current is opposed to that of the polarising galvanic current (Fig. 96, *b*).

It depends essentially upon the magnitude of variation in intensity of the former, whether a twitch is yielded by the muscle, or not. If the line of intensity of the (presumably) very weak, polarising current is represented by a straight line above the abscissa, and running parallel with it, it is evident that while, with uniform direction of excitation current and polarising

¹ Since the disappearance of induced currents does not usually, on account of their extremely brief duration, give rise to a break excitation, we must not hesitate in the cases cited to regard the action of a homodromous induction current as similar to that of a single, rapidly disappearing positive variation of the galvanic current.

galvanic current, the ascending portion only of the superposed curve of variation is concerned in the excitation of the muscle, this is by no means the case when the two interfering currents are opposite in direction. Here, under some conditions, the descending as well as the ascending portion of the curve may have an excitatory effect (Grützner, cf. *Pflügers Arch.* xxviii. p. 146); in the first case excitation would occur on opening, in the second on closing the circuit. With lower intensity of the polarising galvanic current, the first effect would not, however, come into consideration. But the other would also remain ineffective if the battery current is so weak that its closure *per se* produces no visible twitch. So long as the deepest point of the curve of variation has not reached, or only just reaches, the abscissa, the sudden renewal of the momentarily weakened, or interrupted battery current will not induce excitation. It is only when the deepest point of the curve of variation extends below the line of the abscissa, *i.e.* when the intensity of the exciting current is so great that it not merely interrupts the polarising constant current, but a certain fraction of it also traverses the muscle in a direction opposed to the constant current, that a twitch may possibly follow, and to this it must be added that the excitatory process will in this case be discharged at spots that were formerly anodic. Excitation therefore occurs at the points where the constant current enters, not *during its passage*, but at a minimal interval after it has been broken. The return of the polarising current to its original height, which follows immediately after, will not accordingly produce excitation, being too low in intensity. It is easy to see that with greater strength of the battery current, the relations will become yet more complicated, since both its negative variation of intensity, and also its recovery after previous diminution or interruption, may cause excitation.

It follows from the above that the possibility of producing any changes of excitability in anodic points of the fibres by means of an induction current opposed in direction to the polarising current, is connected with very peculiar conditions.

In the first place, it appears to be essential that the intensity of the exciting current should considerably exceed that of the polarising current, for it is only under these conditions that it is possible to conclude with any probability that, during the closure of the latter, that fraction of the induced current remaining for

excitation of the muscle is sufficiently large to provoke a twitch, where the excitability at the anode has remained normal. If, however, excitation was wanting in such a case, we should be fully justified in concluding that there was decreased excitability at the anodic fibre points. Whether in any given case this theoretical assumption is sufficiently justified is the harder to determine, inasmuch as the exciting current differs essentially from the polarising battery current in potential, as well as in variation of intensity—a circumstance which is of great significance to the results of excitation. Brücke's investigations have made it certain that the excessively short duration of induced currents implies a relatively greater intensity in order to excite a curarised muscle to the same degree as the galvanic current under similar conditions. Since it appears consistently that even a very weak battery current (2 Dan. rheochord res. = 1–3 cm.) suffices to inhibit the excitatory action of a heterodromous induction current discharging a maximal twitch, so that no effect can be observed during closure of the battery current even when the exciting current is greatly strengthened, it is surely legitimate to conclude that response from the anodic points is lowered during polarisation.

Summing up what has been said, it follows that if a muscle is continuously traversed by a galvanic current, the excitability of the kathodic points during the passage is found to be either raised or lowered. The former occurs with low intensity of the polarising current, the latter with greater strength, or with longer closure of weak currents. So far as it is possible to conclude from electrical experiments, the excitability of anodic points is always lessened, or completely inhibited, during the passage of the polarising current.

In the next place, what occurs with regard to *excitability of the poles on opening a polarising current*? These "after-effects" may be described shortly. We have already said that after a moderate closure of a very weak electrical current, no after-effect can be determined at the kathode, because the excitatory action of single, homodromous induction shocks, which is considerably heightened during the polarisation, resumes its original proportions so soon as the battery current is opened. If, on the other hand, a battery current of medium intensity is closed for a long enough period (1–2 minutes usually suffices), there is invariably, as in

Series I. and II., a diminution of excitability at the kathode, not merely while the current is passing but also after the polarising current has been opened. This lasts longer in proportion with the intensity and duration of the current. Such a muscle, after prolonged rest, possibly not for several minutes, will recover itself so far that an induction current homodromous with that which exhibited twitches previous to polarisation will again produce excitation. Normal kathodic excitability is, however, much more quickly restored, even when spontaneous recovery is abolished on account of widespread local fatigue, if the polarising current is reversed for a short time. Closely allied with this, also, is the fact that anodic excitability is usually considerably augmented after a not too brief polarisation of a curarised muscle, provided the battery current is of adequate intensity.

Although these manifestations of the so-called "voltaic alternative" have long been known, it has not been sufficiently taken into consideration that this is just as much a polar, *i.e.* purely local, effect of current as in the excitatory process at the kathode. Heidenhain (43) discovered that muscles, the excitability of which had been depressed by any injurious influences (tetanising, protracted passage of current, heat, etc.) to such a degree that they did not react perceptibly even to the closure of very powerful currents, recovered their excitability partially, at least, after they had been exposed for some time to the action of a strong ascending or descending current, excitation occurring again on opening the polarising, or closing a heterodromous current, to a greater or less degree: Rosenthal (44) pointed out the connection between these facts and the phenomena of the voltaic alternative in *fresh*, non-fatigued muscle, which he was the first to investigate.

According to these observations, which are easy to confirm, the response of every muscle sinks, with prolonged passage of current in one direction, towards the closure of such a current, being, on the contrary, considerably augmented for the opening as well as closure of a current in the opposite direction. The first effect, as was shown above, is dependent upon a state of fatigue confined exclusively to the kathodic points.

The experiments which led to this conclusion show, moreover, that the increase in response to closure of a homodromous current, demonstrable after break of an adequate polarising current, is characteristic of the anodic points of fibres.

Since it is a well-established fact that on closure of current excitation occurs only at the point where it leaves the muscle, the proof that excitability increases at the anode *after* polarisation, lies essentially in the fact that the effects of excitation are augmented with closure of a polarising current in the opposite direction. It is conceivable that such changes in excitability might extend over a larger or smaller part of the tract of muscle traversed, although the complete failure of electrotonic alterations of excitability in the intrapolar tract during the passage of the current renders it *a priori* very improbable. Direct electrical excitation of different points in the continuity of a previously polarised muscle, moreover, affords direct proof that just as little as the negative after-effect of polarisation extends beyond the physiological kathode, does the positive after-effect pass beyond the limits of the physiological anode, provided only that the polarising current is not too powerful, otherwise a complex of disturbances might arise through the formation of secondary electrodes.

Undoubtedly the alterations of excitability in question during, and after, the passage of current through a muscle, stand in very close relation with the effects of excitation and inhibition already described, being indeed only another aspect of the same facts. We have seen that when the electrical current acts as a continuous excitation at the kathode, the alterations of excitability, or capacity of response observed are its necessary consequences, and equally under all conditions must we predicate depression of excitability at the anode whenever an existing excitation is inhibited during closure. The complete reversal at break of the polarising current follows as cogently from the reversal of polar manifestations of excitation and inhibition. Since neither excitatory nor inhibitory phenomena are produced by the direct action of current within the intrapolar area, but only appear as changes induced at the poles, or by the effectuation of secondary electrodes, it is *a priori* certain that there can be no question of alteration of excitability within the intrapolar tract by direct action of current in v. Bezold's sense—nor, as we shall see, does any such alteration exist.

Nor is there legitimate ground for assuming changes of conductivity within the intrapolar tract, and the experiments of v. Bezold in this direction can hardly be regarded as convincing. He investigated the effect of polarising a tract of muscle

3 mm. long, upon the conduction of a wave of excitation set up beyond its limits. He found that the conductivity of the polarised section of the muscle diminished in proportion with the strength of current and length of its passage. At a given degree of polarisation, the power of conducting seemed to be completely abolished. (This, *e.g.*, was the case after the current from 4 Dan., with a rheochord resistance of 100, had been sent through a tract of muscle 3 mm. long, for 40 secs.) Von Bezold affirms that the substance of muscle, like that of nerve, is "paralysed" by the current. This paralysis he describes as a defect, or inhibition, of conductivity, although the apparent injury to the muscular tract does not prevent it from being thrown into a state of local excitability by external stimuli as rapidly as before. Von Bezold did not inquire into the reaction of different sections of the intrapolar tract with reference to changes in conductivity, but he inclines to the view "that the curve of defect in the intrapolar tract, as in the parallel case of nerve, sinks from either pole towards the middle."

It is the more advisable in this connection to investigate Engelmann's experiments on the effect of polarisation upon the conductivity of smooth muscle, because while there are manifold analogies between the smooth muscle of the ureter and striated muscle, as regards response to the electrical current, there appear in this instance to be essential differences between the data obtained by the author from striated muscle, and Engelmann's observations on the ureter.

He finds that conductivity in a polarised tract of ureter diminishes in the side towards the anode, and increases in that towards the kathode. The magnitude of the changes is maximal at the poles. The length of the area of depression increases with strength and intensity of current, conduction being finally abolished in the whole intrapolar tract. When the wave of contraction started from a point above an ascending polarised section of the ureter, Engelmann observed that it traversed the entire intrapolar tract—if the polarising current was very weak—though with a marked diminution at the anode. With strong currents the wave disappeared altogether at this point, and with still stronger (persistent contraction at the kathode), it died out even at the kathode.

With regard, firstly, to v. Bezold's experiments, they by no

means prove that the conductivity of *the whole intrapolar tract* is diminished or abolished, it being indeed much too short. The inhibition of the wave of contraction might equally have its seat at the anode, if, as certainly appears from Engelmann's experiments on the ureter, it is true that the conductivity of the muscular substance is considerably depressed there as well as at the kathode, since at the strength of the polarising current employed a persistent contraction must in any case be present, and since, as we may legitimately conclude from Engelmann's observations, a contracted point may, under certain conditions, interrupt the conductivity of excitation.

The next point, therefore, was to test the conductivity of the muscle-substance at the anode as well as at the kathode, and to ascertain its dependence on the strength and duration of the current. For this purpose a strongly curarised sartorius muscle was connected in the usual manner with the unpolarisable electrodes of Hering's double myograph, the centre of the muscle being fixed with oil-clay, and the changes of form of both halves recording themselves on a smoked surface. As a rule, the lower end of the sartorius was excited with single descending make induction shocks. The exciting current escaped by one electrode of the double myograph; its entry was arranged by a loop of thread, moistened with 0.5 % salt solution, and inserted into the clay tip of an ordinary unpolarisable electrode, in order to obstruct the changes of form in either half of the muscle as little as possible during excitation. In the immediate vicinity of the fixed part, corresponding roughly with the centre of the muscle, an electrode of the same kind enabled the polarising battery current to leave or enter the muscle, the whole upper part of which was traversed. A wave of contraction discharged at the lower end of the sartorius traverses the fixed part without interruption, and both halves of the muscle shorten, as a rule, approximately so long as the polarising circuit remains open. Even a weak galvanic current (ascending or descending) passing through the upper half of the muscle continuously, exerts no perceptible influence on the size of twitch in either half. When, however, the intensity of the polarising current is raised (to about 2 Dan. = 100 R.), the kathode being in the centre of the muscle, a pronounced inhibition, in proportion with the strength and direction of the current, in every case interferes with the propagation of the

wave of contraction initiated in the non-polarised section of the muscle. In the first place, it is seen that the two halves of the muscle do not, as before, contract equally, inasmuch as the curves of twitch in the polarised half become smaller and smaller during the passage of current, while on the directly-excited half they remain unaltered. Finally, with renewed excitation of the non-polarised half of the muscle, changes of form on the farther side of the fixed spot fail altogether; the wave of contraction is unable to get past the kathode.

According to v. Bezold we should expect that the whole intrapolar tract would by this time have become incapable of conduction. This, however, is emphatically contradicted by the circumstance that when the polarising current enters at the middle of the muscle, *i.e.* when the anode is at that part, there is never, even on applying very strong galvanic currents, and prolonging the passage of current indefinitely, any perceptible impediment to the propagation of a wave of contraction; sometimes, as we shall see, the direct contrary. There can therefore be no doubt that fibre-points which have served for some time as the exit of a sufficiently strong electrical current, fall into a condition in which they become incapable of propagating a wave of excitation from one side to the other of the section. This impenetrability of the kathode has also been established for nerve by Hermann and Werigo (*infra*). The conditions of its development are precisely similar to those of muscle.

That it is not the persistent closure contraction, localised at the kathode *as such*, which interferes with propagation, is seen (apart from the fact that both halves of the muscle frequently contract equally, although at the kathode, in the centre of the muscle, there is also a marked continuous contraction), in that the inhibition is most pronounced when a persistent descending current in the upper half of the muscle has reduced the original persistent closure contraction to a minimum. It is therefore legitimate to assume that the local *fatigue* of muscle-substance produced by current at the kathode is the fundamental cause of the inhibition of conductivity in that region. With regard to the above observations on the rapid decrease of response at cathodic points during polarisation, it might appear strange that with the given experimental conditions the inhibition of conductivity at the kathode is first exhibited at a comparatively

late period after the closure of fairly strong currents. The cause of this deviation is presumably to be sought in the different mode of exit of the current in either case. For while in the first case this occurs at the *ends* of the fibres, in the other the "physiological kathode" lies at the centre of the muscle, where current density must be less on account of the larger section; while, on the other hand, the oblique course of the isolated lines of current directed towards a small zone of the muscle surface causes the innermost fibres to be less strongly excited than those at the periphery, since the current leaves the former with a less density than the latter. Accordingly we always find that when the exit of the current occurs, as described above, at the centre of the muscle, much stronger currents will, as a rule, be required to produce a make twitch than under the opposite conditions. So long as the total section of the muscle at the exit of the current is not fatigued by prolonged passage of current, each wave of excitation arriving at the kathodic section will endeavour to pass beyond it, since it can—so to speak—glide under the most strongly excited peripheral zone, and is first completely inhibited when the muscle is, if we may so express it, functionally separated, *i.e.* divided by a small unexcitable zone into two excitable sections, from the continuance of the state of local excitation. This separation makes it conceivable that, as a rule, tolerably protracted polarisation by fairly strong currents is required in order to depress conductivity at any point in the continuity of the muscle to such a degree that an approaching wave of excitation will be hindered in its progress. If the upper half of the muscle, as we have been assuming, is polarised in a descending direction, and the current then suddenly reversed, the vigorous make excitation discharged at the previously anodic end of the muscle, fails to pass beyond the section which has been rendered incapable of conducting by the sustained excitation at the kathode, and at closure only the directly excited and formerly polarised half of the muscle will twitch, while the other half beyond the fixed part remains passive.

Conductivity is recovered, under certain conditions, when the current is broken; but if it has been too strong, or if polarisation is prolonged unduly, the kathodic section may remain permanently incapable of conducting.

We have seen that, contrary to the behaviour of the ureter as observed by Engelmann, the conductivity of striated muscle (sartorius) exhibits no perceptible diminution under the influence of the anode. This is the more striking since there is complete agreement in both cases as regards *direct* excitability. And it is further less likely that there should be any fundamental divergence between the two cases, since anodic inhibition of conductivity is very pronounced in nerve also. The difference must be due simply to external factors, among which may be instanced the thickness of muscle and transverse course of the lines of current. The fact above alluded to, that kathodic inexcitable points may be so modified by the influence of the anode as to become capable of excitation once more as soon as the electrical current leaves the muscle at the points in question, only show that they have again become sensitive to direct electrical excitation. But since we may conclude from this that alterations of muscular excitability by no means invariably entail corresponding alterations of conductivity, it is conceivable that, notwithstanding the restoration of direct excitability, the power of conduction, *i.e.* of being thrown into excitation indirectly by a wave of contraction from some other point, may sometimes be permanently abolished at the kathode. Experiments with passage of current through one half of a curarised sartorius indicate, however, an opposite result, *i.e.* even in cases where polarisation has been so long continued that there can be no question of spontaneous restoration of the now incapable muscle section, the power of propagating the excitatory process has been invariably and even permanently restored under the influence of the anode, provided the current used be sufficiently powerful.

In this way it lies in our power to render any given section of a muscle with parallel fibres permeable or impermeable to a wave of contraction from without, according as we make the current traversing one half of the muscle enter, or pass out, at the centre of the muscle.

As regards alterations of excitability in a polarised muscle, we have direct proof that whether extra- or intrapolar they do not extend beyond the physiological kathode or anode, and there is no reason to infer the opposite for alterations of conductivity. All the evidence, on the contrary, goes to show that the one as well as the other must be regarded strictly as a *polar* effect of current.

THE ELECTRICAL EXCITATION OF UNFIBRILLATED PROTOPLASM

The action of the electrical current upon muscle has long since attracted the attention of physiologists; the consequences of the passage of current through unfibrillated protoplasm (which are of the greatest interest in a theoretical connection) have until lately been almost entirely disregarded, and only a few isolated observations indicate that we are here concerned with facts of wide-reaching significance.

In connection with certain theoretical views as to the causation of plasmatic movements—of the streaming movements in vegetable cells in particular—Bequerel examined the effect of a strong current flowing through a spiral wire round a decorticated cell of Chara. No effect was produced, whether the axis of the wire-coil was parallel, or at right angles, to the axis of the cell. Later experiments were equally negative; no *action at a distance* of the current upon any sort of excitable protoplasm could be detected, so that it may be taken as certain that such an action, generally speaking, does not exist.

In consequence of the direct action of weak induction currents, Kühne and Engelmann observed the movement of Amœbæ to be at first arrested and then resumed after a short time. With stronger induction shocks the Amœbæ assumed a globular shape by the withdrawal of all their pseudopodia, which at once arrested all molecular movement. Finally, with very strong excitation the sphere of protoplasm may collapse and extrude its endoplasm, which is equivalent to the total destruction of the animal (45).

Rhizopods with numerous long and slender pseudopodia withdraw these when electrically excited, and in this case it is especially remarkable that *those pseudopodia which lie at right angles to the lines of current show no change, or at any rate change only with far stronger currents than those which lie parallel to it*, a fact which calls to mind the similar behaviour of muscle under similar conditions. Kühne (46), when tetanising Actinosphaerium with the alternating currents of an induction coil, observed that the pseudopodia *lying along the line between the two electrodes* soon became varicose; the granular protoplasm along the axial ray gathered itself into little spheres and spindles, which flowed towards the

body, while the entire pseudopod was gradually withdrawn. Since we shall frequently have occasion to refer to these rhizopods (which are exceptionally well adapted to electrical excitation experiments) it is advisable here to introduce some further remarks as to their structure. The fairly large globular body of *Actinosphaerium* exhibits two distinct layers—a darker, central, richly nucleated mass (endoplasm), and a lighter, vacuolated, cortical layer (Fig. 97). Each vacuole is filled with fluid, bounded by a wall of homogeneous, finely granular protoplasm;

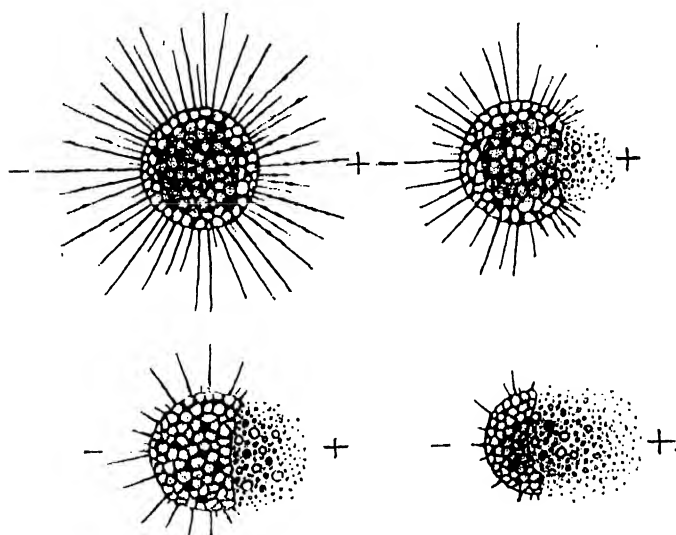


FIG. 97.—*Actinosphaerium eichorum*. Polar effects of excitation with passage of a constant electrical current. (Verworn.)

this same protoplasm forms part of the bristle-shaped pseudopodia which stand out from the body in all directions, and exhibit a characteristic differentiation of structure—an “axial ray” of firmer consistence covered by the somewhat fluid protoplasm like a rind.

The contraction phenomena described by Kühne manifest themselves in a constant manner to a given mode of excitation. “In consequence of stimulation the axial ray of a pseudopod in the unexcited state of almost homogeneous enveloping protoplasm, gathers itself together, while streaming towards the body upon the axial ray, in small, solitary, fusiform or globular varicosities, between which

the axial ray lies completely bared at many points. The spindles and spheres glide slowly upon the axial ray (which at the same time is being withdrawn into the body), in a centripetal direction, sometimes coalescing, and finally flowing entirely into the protoplasm of the cortical layer." If the excitation is strengthened, or prolonged continuously, the fluid vacuoles of the cortical layer begin to collapse, after the pseudopodia have been withdrawn from the excited spot (or may be from the entire body), because the protoplasm which forms their walls shrinks more and more inwards. This gives to the body an irregularly-bounded, lumpy surface. Finally, with still stronger excitation, the protoplasm begins to disintegrate into granules, by a gradual process beginning at the surface, and progressing slowly inwards until the central mass is involved, when—unless the excitation is stopped—the entire body is destroyed. Short of such total disintegration it is possible for the undestroyed remainder to reconstitute itself into a perfect, though correspondingly diminished *Actinospharium* (Verworn, 47). With sufficiently strong excitation the plasmatic bands and threads of certain vegetable cells (*Tradescantia*) will comport themselves like the pseudopodia of rhizopods. With weaker excitation there may frequently be observed, as in the case of independent amoeboid protoplasm, a slowing and arrest of the spontaneous streaming movements, followed by the formation of varicosities, lumps, and so forth, upon strengthening the excitation. Kühne observed that these effects were localised to a restricted portion in correspondence with localised excitation. If a large cell of *Tradescantia* is arranged transversely to a pair of fine-pointed electrodes lying close together, it is possible to send currents of great density through a limited part of the cell. With gradual approximation of the secondary to the primary coil the movements of only a portion of the cell are arrested, and a formation of swellings, lumps, and knots ensues, which may be subsequently reinvolved in the stream of the intact protoplasm. The circulating plasma of *Vallisneria*, *Chara*, *Nitella*, etc., when submitted to electrical excitation, always exhibits a retardation and subsequent arrest of the streaming movements.

The phenomena exhibited by certain kinds of protoplasm, when submitted to the action of the constant current, are of far greater interest. The first observations in this direction are due to Kühne, who, as long ago as 1864, drew attention to the re-

markable and in many respects important reactions of Actinosphærium to the galvanic current. We shall in the main follow the account given by Verworn (*l.c.*) who has recently repeated these observations, completing and extending them in various directions. In regard to method it should be observed that unpolarisable electrodes were exclusively employed in these experiments. The Actinosphærium is placed in a few drops of water in a little excitation chamber, made by cementing two slabs of porous clay, joined by two transverse partitions of cement, on to a large object glass, so as to form a (closed) rectangular space, to the clay sides of which brush electrodes were applied, so that current could traverse the chamber in approximately parallel lines. In consequence of the high resistance in the circuit, comparatively high electromotive force must be used in order to obtain distinct effects, which, however, in such cases are perfectly characteristic. At closure of the current, in the first place, the pseudopodia, both on the anodic and kathodic side of the globular body, become varicose, and begin to contract as described above; *whereas the pseudopods that are situated at right angles to the line of current exhibit no changes.* On the kathodic side the effects of excitation are comparatively inconsiderable and very evanescent; the pseudopodia soon resume their normal aspect. *The corresponding effects on the anodic side, on the contrary, proceed uninterruptedly as long as the current is passing.* Little by little the pseudopodia are completely withdrawn; the vacuoles in the cortical layer begin to collapse and empty themselves of fluid; a gradual dissolution of the body-mass takes place on the anodic side, while the protoplasm disintegrates into granules. In this manner a concave gap is gradually formed on the anodic side, while a very slow retraction of pseudopods is taking place over all the rest of the body. Finally, the Actinosphærium becomes sickle-shaped like a new moon, the greater part of the body-mass having undergone disintegration into granules (Fig. 97).

If the circuit is opened at a moment when the pseudopodia are still in a normal state, except on the anodic side, the corrosion at the anode ceases directly, and the pseudopods on the kathodic side become varicose in about the same degree as had taken place immediately after the closure of the circuit. This effect is, however, very evanescent; the pseudopods soon recover their normal aspect, while the anodic gap gradually fills up at the same time,

and a complete individual is formed again, although on a smaller scale. With weaker currents the process generally stops short of the collapse of vacuoles, only the gradual retraction of pseudopodia on the anodic side is produced; and there is no sign of any kathodic break effect. The rapidity with which all the above-described phenomena develop is greater with increased strength of current. At closure of very strong currents the granular disintegration on the anodic side begins almost instantly, and then progresses more and more gradually towards the centre as long as the current is passing.

According to Verworn the slow retraction of pseudopods on the general body-surface that takes place during a prolonged passage of current is to be regarded as a secondary process, arising from the disintegration that has just taken place at the anode, and stimulates the protoplasm, inasmuch as it always commences after a considerable loss of substance has become apparent.

From the above-described changes we may easily predict the consequences of *alternating currents*. With moderately frequent stimuli the pseudopodia at both poles begin to exhibit varicosities, and also with stronger currents the granular break-down proceeds *pari passu* from both sides. It is worthy of note that *with very rapid reversal of current, effects that are in progress become arrested, to recommence with the adoption of a slower rhythm*.

Verworn pointed out that *Polystomella crispa* — a marine Foraminifer with numerous very fine pseudopodia, forming a complex and retiform anastomosis, upon which the phenomena of "granular currents" described by Max Schultze are well exhibited — reacts in precisely the same way to the constant current. "At make of a current all the granules in the pseudopodia of the anodic side begin to flow in a centripetal direction, and at the same time are slowly retracted, and the longer the excitation continues so much the fewer and shorter are the pseudopodia which protrude from the cortex, until before long there is a total disappearance of pseudopods on the anodic side." On the kathodic side no such change is visible, the streaming of granules goes on as usual, and the pseudopodia remain extended;—"they may even lengthen considerably, or make their appearance at closure of the current at a kathodic area previously free of pseudopods, the flow of granules being now in a centrifugal direction." In this case, as before, no change could be observed at or after closure of the circuit in

such pseudopodia as lay across the lines of current. Verworn was unable to detect any definite cathodic break effect.

The excitation changes that are observable under similar conditions in *Pelomyxa palustris* are of no less interest. *Pelomyxa* is a solid mass of naked protoplasm, often as much as 2 mm. in size, which is rendered very opaque by the large quantity of sand and mud englobed by the animal. The movements are extremely sluggish, and, as in many *Amœbæ*, consist in a flow of the endoplasm along the body-axis in a given direction, with a bending round and backward flow along both sides. In this way a blunt process in the direction of the axial current is formed, at the margin of which a hyaline border is often distinguishable. Excitation produces a variety of effects according as it involves the entire surface, or is localised to one spot, and is strong or weak. "Weak prolonged stimuli acting upon the whole body, *e.g.* vibrations, produce a very gradual but complete balling of the body. Weak localised stimuli produce a gradual withdrawal of the excited part. Strong stimuli (*e.g.* by chemical reagents) acting upon the body likewise produce a spherical rounding, while at the same time there is an escape of the granular endoplasm, in consequence of the disintegration of the outer protoplasmic coat—this escape is partial with localised excitation. The granulated, disintegrating protoplasm bursts out, and the appearance is the same as when *Actinosphaerium* is submitted to the action of strong currents." A sufficiently strong galvanic current acts upon *Pelomyxa* with the same results (Fig. 98).

At closure the contents of the body burst forth on the anodic side, and as in *Actinosphaerium*, the disintegration spreads more and more in the direction of the kathode, until the last trace of protoplasm has disappeared. This process of disintegration passes with diminishing rapidity from the anode to the kathode in about $\frac{1}{2}$ to $\frac{3}{4}$ minute, with currents of equal efficacy, at the end of which period the individual is completely abolished. At first the process is extremely sudden, then slower, until it gradually becomes imperceptible. It passes over the whole body in the form of an annular constriction, starting from the anode and advancing towards the kathode; that portion of the body-mass which is on the anodic side of the constriction, *i.e.* which has been traversed by it, is in a state of granular disintegration; that portion which is on the kathodic side is still normal and

living. "If the current is *broken* when the process of destruction has involved only a small portion of the entire mass, the disintegration ceases to progress, whilst a swelling of granular disintegrated protoplasm suddenly breaks out at the kathode, similar to that which appeared at the anode at the closure of the circuit. But this process at the kathode makes no further progress after the opening of the circuit." The smallest undestroyed portion of protoplasm is sufficient to form a new individual on a smaller scale. With weaker currents the anodic effects may be preceded by a long, latent period (1 minute or more). On *Pelomyxa*, according to Verworn, the action of induced currents, and of con-

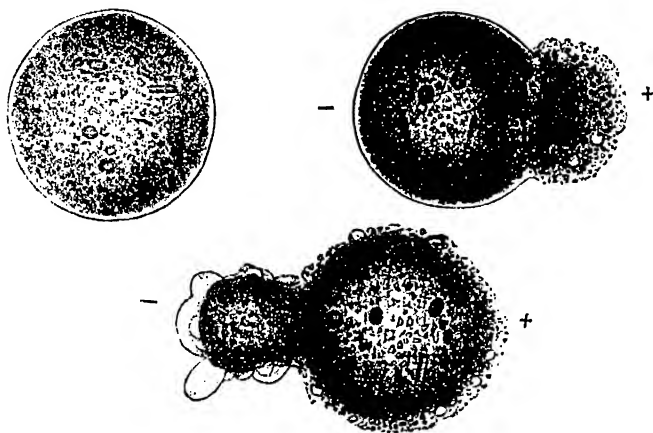


FIG. 98.—*Pelomyxa palustris*. Polar excitation effects with passage of a constant current (Verworn.)

stant currents of brief duration, is particularly striking; at a given current strength only a *kathodic break excitation* is obtained, whereas with currents of longer duration an *anodic make excitation* makes its appearance. The effects are thus contrary to those obtained on muscle, not only as regards the law of polar excitation, but also as regards the manner in which make and break excitation depend upon the duration of the exciting current.

Various forms of *Amœba*, investigated by Verworn (*A. limax*, *verrucosa*, and *diffuens*), exhibited some apparently considerable divergences from the phenomena observed on *Pelomyxa*: at any rate with the strength of current made use of, instead of the destruction of the anodic pole of the body, a protrusion (formation of pseudopodia) was produced at the kathodic pole. At make

of the constant current the first effect is usually a momentary arrest of the flow of granules, followed by the sudden protrusion of a hyaline pseudopod from the anterior end of the body, directed in a straight line towards the kathode. In the case of *Amœba limax* this powerful pseudopod extends to a considerable length, and draws the entire body-mass into itself, so that the amœba following the direction of current creeps towards the kathode by degrees, in its normal form. If the current is suddenly reversed during this period, the flow of granules and the progress of the amœba are reversed in direction—with a strong current—and it is possible by frequent alternation to obtain continuous movements of the amœba in opposite directions. It is easy to show that the action in this case is essentially similar to that witnessed in *Actinosphaerium*, *Polystomella*, and *Pelomyxa*, although obvious signs of excitation cannot be detected. If, as can hardly be disputed, we may reckon as effects of excitation the formation of varicosities in the pseudopods, along with their retraction, and the eventual partial destruction of the body-substance, two important conclusions may be deduced from the observations before us. In the first place, the proposition follows, that, *like muscle, the substance of protozoa obeys a law of polar excitation, in which, however, the localisation (polar distribution) of effects is reversed—excitation being at the anode at make, at the kathode at break, of current.* Secondly, the fact carries conviction, *that the process of excitation is effected not merely at the moment of commencement and cessation of current, but proceeds throughout the whole period during which the current is passing, and for a short time after it has been broken.* This excitation does not produce contraction as in muscle, but sets up a centripetal backward flow of the protoplasm, which under certain conditions may lead to local destruction of the outermost layers. The various phenomena connected with the final disintegration in various forms are sufficiently intelligible from the different composition and consistence of protoplasm in each particular case. Under certain conditions—*e.g.* in *Amœba*—visible changes of form are altogether absent; *the excitation remains "latent."* But even then the direction of movement of the entire body-mass gives cogent evidence of the existence of polar excitation, and it is quite intelligible that such excitation should, under certain conditions, give rise to an axial disposition of the body of the proteid. In the first place, we find that other

stimuli, *e.g.* light, warmth, chemical reagents, are known to exercise a directive influence, if they act *locally*, or with different intensity at different parts of the excitable substance. Certain light rays (those with short vibrations in particular) cause many of the Flagellata, as well as the spores of many Algae, to move in the direction of the rays that strike them, either from or towards the light (positive and negative heliotropism). Pfeffer has demonstrated an analogous effect of chemical reagents in solution upon Bacteria and Flagellata, *i.e.* attraction or repulsion of the organisms, a chemotropic action positive or negative. In all these cases, as Verworn correctly remarks, we have to do with some polar excitation of the protozoa, that gives rise to an axial orientation of the organism in accordance with the direction of excitation, or, more correctly speaking, of the differences in intensity of such excitation. On the assumption that when current passes through an amoeba, the make excitation, as in other rhizopods, is primarily anodic, it is evident that a formation of pseudopodia due to a forward current of the protoplasm can take place only in the direction of the kathode; the forward movement in the direction of the current is thus accounted for.

This directive action of the current ("Galvanotropism") is still plainer in the case of many rapidly-moving ciliated Infusoria, *e.g.* Flagellata. If a few drops of hay infusion swarming with paramacium are placed between clay electrodes (as described above) upon an object-glass, and traversed by a sufficiently strong current, the following effects (as pointed out by Verworn) are observed, either with the naked eye or with a magnifying lens. "At closure the Paramaecia turn altogether as if at word of command, with the anterior pole of the body towards the negative electrode, and swim in this direction with uniform speed" (Fig. 99).

In a short time the anodic side of the drop is completely cleared of Paramaecia, not one being left behind; the whole mass has crowded to the kathode. As long as the circuit is closed the protozoa remain thus; if the current is broken the paramaecia turn instantly with their anterior ends towards the anode, and swim away in this direction. The kathode is quickly deserted, and the majority of the organisms are now collected round the anode. The crowding is, however, by no means so complete as that produced at the kathode by make of the current, and the

paramæcia soon begin to swim about in all directions, and in a short time are once more uniformly distributed throughout the drop. This manœuvre is repeated as often as the current is closed, with the same precision.

It is easy to prove that the living state is an essential condition of these phenomena by repeating the experiment after killing the animals with ether or chloroform.

If unpolarisable electrodes are used with points of baked clay dipping into the infusion, instead of the excitation chamber

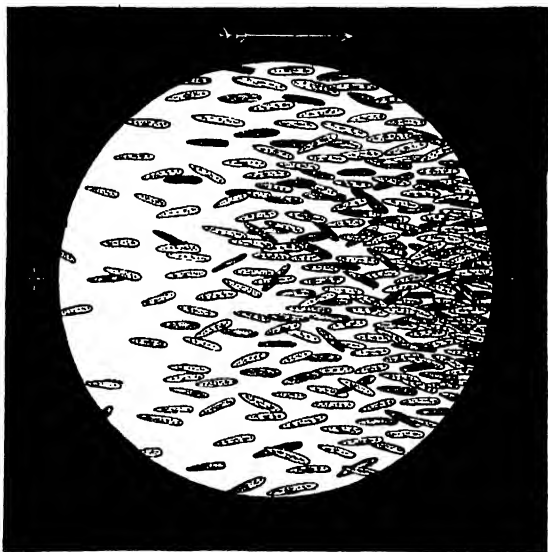


FIG. 99.—Galvanotropism of *Paramacium aurelia*. (Verworn.)

described above, the effects are very curious. At closure of the current all the paramæcia arrange themselves longitudinally, in accordance with the current curves, and swim along these lines towards the kathode, so that those which happen to be at the outer part of the drop follow an almost semicircular course. If the current is frequently reversed, the paramæcia may be driven now in one direction, now in the other. As may readily be understood, very rapid alternations of current do not cause them to travel in a definite direction, nor give rise to any polar accumulation. *A priori* there can be no doubt that in this case, as in that of *Amœba*, we have to do with a "galvanotropic

action" due to latent make excitation at the anode; and the fact itself is directly demonstrable by corresponding experiments on other infusoria less resistant to the action of current than *Paramaecium aurelia*. On *Paramaecium bursaria* (the galvanotropic reaction of which to weak currents is as well marked as is that of *Paramaecium aurelia*), Verworn, using strong currents, succeeded, as in the case of the above-mentioned rhizopods, in producing a visible destruction of one pole of the body, *i.e.* of the anodic pole, that is posterior when swimming takes place. At closure of the current the first effect is as usual an axial orientation, and subsequently as the proteid begins to swim over towards the kathode, a hyaline mass protrudes from the posterior end and gradually enlarges. It can hardly be doubted that this is analogous to the anodic disintegration that occurs in *Actinosphaerium* and *Pelomyxa*. It is still easier to bring about a similar reaction in the case of *Bursaria trunculata*; moderately strong currents are sufficient to effect a granular disintegration of the anodic end of the body, which increases as long as the circuit remains closed, until the whole animal is converted into a granular mass loosely held together by glutinous material. These large and more resistant infusoria have no time to adjust their axis, especially with strong currents, but the destruction begins at any aspect of the body which happens to be turned towards the anode at the moment of closure (Verworn).

A large number of other ciliated Infusoria, also some of the Flagellata (*Peridinium tabulatum* and *Trachelomonas hispida*), as investigated by Verworn, behave in a similar manner. On the other hand, in some other protozoa, the current produces a precisely opposite directive effect. If the swimming or crawling movements towards the kathode be designated as *negative galvanotropism*, the reverse effect (anterior end to anode, and movement in that direction) may be called *positive galvanotropism*. Verworn found this last-named effect in *Opalina ranarum*, also in certain Flagellata, *Polytoma uvella* and *Cryptomonas crosa* in particular. The phenomenon described by Verworn as "*transverse galvanotropism*" is, moreover, remarkable; certain very elongated Infusoria (*e.g.* *Spirostomum ambiguum*, 2 mm. long) place themselves with their long axis at right angles to the lines of current (perhaps in consequence of a failure of excitation by transverse currents). Apart from these isolated cases, which require further

study, it is allowable to suppose that the proposition laid down above with reference to the electrical excitation of protozoans holds good for the great majority of the forms hitherto investigated, thus establishing in their case a peculiar and unquestionably very remarkable opposition to the phenomena of muscular elements in general, as well as of nerve. The allied assumption that the law of polar excitation, according to Pfüger, holds good without exception for all excitable protoplasm, thus appears to be finally disposed of.

The interesting observations of Roux (48) upon "*morphological polarisation*" of ova are germane to the phenomena described in the foregoing pages. In order to determine whether the electrical current was capable of influencing the direction of the first cleavage of the ovum, Roux submitted a strip of frog's spawn about 4 cm. long, with fertilised ova, to the action of an alternating current of 100 volts potential, intended for lighting purposes. In about ten minutes a transverse furrow dividing the egg into two equal parts appeared in each egg, the furrow being everywhere at right angles to the direction of current. Even before this happens a distinct partition of the surface into three fields is noticeable, divided off by two parallel circular boundary lines, an equatorial girdle without visible alteration, and two polar areas opposite the electrodes, with an altered and coloured surface. If instead of a single band of spawn a simple layer covering the bottom of a round vessel is submitted to the action of the current, the electrodes being placed at its two opposite margins, the equatorial girdle of the entire series of eggs, or, more precisely speaking, the boundary lines between it and the polar zones, form curves which all begin at right angles to a straight line between the electrodes (Fig. 100), and then sweep round the nearer electrode, gradually increasing their distance from it as they approach the wall of the vessel, to end at right angles to the same.

The amount of curvature is at its maximum close to the electrodes, and gradually diminishes up to the middle line, at right angles to the current axis. The merest inspection shows us that we are here dealing with lines of equal potential, or the equipotential surfaces of the whole electrical field marked out by these. In the ova corresponding with a single line of potential, the breadth of the equatorial surface increases with

its distance from the straight line between the electrodes, so that the ova in immediate contact with the margin present the least polar zones, and the largest equatorial surface. Bearing in mind the reaction of each single ovum to the alternating current, a certain analogy with the effects above described in *Actinosphaerium* cannot be disputed, and if two protozoa are conceived—of the size of frog's ova, and submitted under similar conditions to the action of the alternating current—the middle disc remaining over, when the polar zones had disintegrated, would presumably exhibit an arrangement of the lines of potential, corresponding with the equators of the ova in Roux's experiment.

But this conformity further extends to the difference in mode of action at either pole, which of course appears only with uniform currents. At uniform conditions of experiment, there is developed—as Roux pointed out—in ripe, unfertilised ova, “a large grayish polar zone, round the positive electrode, *directed towards the anode*, extending far beyond the middle line of the electrical field, while

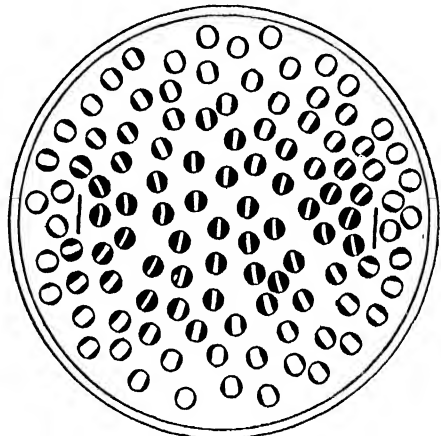


FIG. 100.—Ova of Frog in vessel of water, traversed by current from the two straight lines, marking the vertical electrodes. Polar fields dark. (Roux.)

only the two rows of ova lying nearest the kathode had a coloured cathodic polar zone in default of an anodic zone.” This last always appears later, and the changes are less than in the positive zones. With weaker currents, no polar zone appears on the negative side of the ovum.

If these effects of current cannot be termed direct consequences of an electrical excitation of the plasma of the ovum, they do undoubtedly represent a specific reaction of the still *living*, or at least approximately normal, ovum, even when the capacity of development is not necessarily preserved. Roux was enabled to demonstrate formation of polar zones in masses of freshly extruded unsegmented ova.

The reaction of ova, which are already at different stages of segmentation, is also interesting. Both in the ovum divided into two or more cells (Fig. 101), as in the morula stage, and again in the blastula, consisting of many little cells, each single cell of the surface shows "special polarisation" when the whole organism is submitted to current, inasmuch as "the cells lying only on the polar side of the ovum exhibit *one* polar zone, which is visible externally, while the equator takes up the free surface of the cell lying distal to the pole." Further differentiation into smaller and fewer cells, in older blastulae and the gastrula, will, however, under the same conditions, once more bring about a collective equator between two collective polar zones, since a girdle from the poles to the farthest cells remains unaltered. The special polarisation of single cells in the early stages of segmentation would appear to be "bound up with a property



FIG. 101. — "Special polarisation" of an ovum in four segments, submitted to action of strong alternating currents. (Roux.)

which diminishes with their vitality," inasmuch as each attack which weakens the vital energy of the ovum also prevents the formation of special polar zones, wholly or partially, without, however, effecting the characteristic "total polarisation" of the entire cell aggregate. Thus Roux remarked in segmented ova treated with weak carbolic acid, which produced no change of form externally, that while special polar zones appeared at the first moment of action of the current, they spread rapidly over the whole surface of the cell directly exposed to the current, so that on each side "a *single* polar zone, springing, however, in the upper hemisphere from rounded cells, appears; while the "general equator," marked off by two parallel sectors, lies between them. With stronger application of the acid there is no reaction. Similar changes are effected by various temperatures.

If unsegmented ova, or morulae, are left in water for a *short* time at 39–45° C. the reactions are considerably increased, while longer exposure to heat has an opposite effect—the morulae no longer exhibiting special polar zones, but only the two "general polar zones" separated by *one* equator. These results, along with the further fact, that on cooling the ova the reaction to current is considerably retarded, indicate that we are in presence of a vital phenomenon, of which the further investigation promises

to contribute largely to our knowledge of the nature of the polar working of the current.

SUMMARY

Gathering up the results of these detailed investigations into the visible effects of electrical excitation in different contractile substances, certain points of view present themselves from which it appears possible at least to conjecture the specific action of current.

In the first place, it must be remarked that the *law of excitation* which du Bois-Reymond postulated as universal (only, it is true, with regard to the electrical excitation of motor nerves, but which was subsequently applied to the *direct* excitation of contractile substances also) is not found to be a correct representation of fact. It cannot therefore be taken as the basis of theoretical conclusions in regard to the specific nature of electrical excitation. The law in its original form was as follows: "The motor nerve (or muscle, contractile protoplasm) responds by the twitch of the muscle belonging to it (or other excitatory symptom), not to the absolute value of current density at the moment, but to the alterations of this value from one moment to another—the stimulus to movement consequent on these changes being greater in proportion to their rapidity at uniform magnitude, or amount per unit of time."

Even if we admit that in many cases, particularly in all quickly reacting and quickly conducting contractile substances, the effect of excitation (so far as it is expressed by visible change of form) is especially prominent at the moment when current is made or broken (closure and opening twitch), there cannot on the other hand be the slightest doubt that the electrical current in every case produces *during its entire closure* that change in the irritable substance which is fundamental on the one hand to excitation, and on the other to antagonistic inhibitory processes. In many cases these continuous effects are the only consequence of electrical excitation (*e.g.* smooth muscle, many protozoa). Currents of insufficient duration are ineffective, as may be demonstrated on striated muscle by the application of various methods (*supra*). Under all conditions the current, in order to excite, must have a certain period of duration—greater in proportion with the

lower excitability and slower reaction of the protoplasm in question. And as at make of the current the excitation by no means accompanies the moment of closure only, so too at break the opening excitation considerably outlasts the disappearance of the current.

The capital importance attaching to the manifestation of the make and break twitch in striated muscle, with regard to the entire theory and discussion of current action, renders it advisable once more to raise the question of what conditions are essential to the initiation of a wave of contraction. We know from experiment that in order to produce a wave, *i.e.* a perceptible twitch of the entire longitudinally traversed muscle, the *magnitude of the stimulus* must exceed a certain minimal limit. If the stimulus is too weak the contraction either remains localised, or spreads over a limited area only of the muscle by conduction from section to section, until it finally dies away in consequence of the "decrement." The second condition essential to the propagation of excitation is a certain rapidity of process of the required magnitude. The changes at the seat of direct excitation must suddenly reach a corresponding magnitude, after which excitation transmits them to the neighbouring sections, and these in turn produce the same effect upon their neighbours. That this is so is proved directly by the fact that it is easy to pass a strong galvanic current into a muscle without any *visible* excitation phenomena, which no doubt is partly due to the gradual increase of local fatigue at the kathode. This applies not merely to the electrical make and break twitch, but to many other experiments. We need only refer to the fact that mechanical excitation caused by pressure does not produce a muscle twitch if it is increased gradually.

This all throws light upon the true significance of du Bois' law of excitation, since it shows that not merely the *local* changes at the seat of excitation, but still more the *propagation* of the excitatory process, *i.e.* the discharge of a wave of excitation (contraction), are dependent upon the *variations* of current intensity, and the steepness of the same, in the case of tissues in which conductivity is adequately developed. The "universal law of excitation" refers therefore less to the manner of the excitatory process, and effectuation of the changes of the excitable substance fundamental to it, *at the*

seat of direct excitation (physiological anode and kathode), than to the conditions of the propagation of the excitatory process by conduction. In this sense the law may be expressed as follows :—

As a rule, when current is applied to suitable objects, transmission of excitation from the point directly stimulated occurs only with sufficiently rapid alterations of current, whether starting from zero, or from any given value.

Comparative investigation of different contractile substances shows directly that visible changes arise at the point of excitation during the entire passage of current, and for some time after, the significance of which is clear except in cases where, *e.g.* in striated muscle, they are more or less overshadowed by the results of the transmitted excitation ("twitch"). Without entering into the question why there is, as a rule, only *one* wave of contraction at closure, and opening, of the circuit, it may be pointed out that the same effect occurs under certain conditions with intermittent persistent excitation from homodromous, rapidly interrupted currents, just as in other cases the continuous closure of a battery current will produce a persistent excitation of the entire muscle similar in appearance to that caused by intermittent excitation. As regards the first, it was shown by Bernstein and Engelmann that when the interval between two consecutive closures of a rapidly interrupted battery current, falls below a certain value, the effect of excitation upon striated muscle is similar to that produced by closure of a constant current; *i.e.* a single wave of contraction (initial twitch) starts from the kathode, at which, as in persistent closure, there may be persistent local contraction. The magnitude of this interval diminishes with increasing strength of current, and increases with diminishing excitability.

The same fact is still more easily demonstrated, according to Engelmann, upon the sluggishly reacting ureter, since the pauses between two consecutive closing stimuli may be much greater than in striated muscle without alteration of the effect, inasmuch as a wave of contraction only occurs at the beginning and end of the intermittent excitation, starting in the one case from the kathode, in the other from the anode ("initial and final twitch"). Under all conditions a certain interval, varying greatly in different contractile substances (where conductivity is in general more highly developed),

is required before, when one wave of contraction has expired, those conditions are restored which are essential for bringing about a new wave of excitation (Engelmann).

The facts submitted above *re* discharge of a rhythmical succession of contraction waves during protracted closure of a battery current, do not contradict this conclusion. Expressed in general terms, the recovery of an original state of the excitable, conducting substance takes place only when a new wave of contraction passes during the continuance of an uninterrupted stimulus.

Yet, in so far as the ratio and time-relations of the assimilatory and dissimilatory processes in living matter are correlative, this would apply to intermittent, as well as to uninterrupted, causes of excitation. As regards the latter we need only refer to the wide distribution of rhythmical processes of movement, depending, as may be shown, in many cases upon the capacity of certain kinds of protoplasm to convert a constant stimulus into rhythmical excitation. This capacity is more or less developed from the relatively undifferentiated protoplasm of protozoa (contractile vacuoles) up to striated muscles, but with striking differences of degree. Thus the non-ganglionated, cardiac muscle pulsates rhythmically not merely with uniform mechanical or chemical stimuli, but also under the action of the constant current, and the same applies, though in a much lesser degree, to striated skeletal muscle. Without entering on the question of the specific cause of the rhythm in these and similar cases, we may point out that the occurrence of a rhythmical succession of contractions during sustained closure of the current is a very convincing proof that the excitation process is persistently maintained during electrical stimulation. The electromotive effects of sending current into the muscle, known, after du Bois, as secondary electromotive manifestations (which will be discussed below), are also of great importance in this connection.

The second fundamental proposition is the law of the *exclusively polar action of every ordinary electrical current, to the effect that the excitatory process is primarily discharged at the physiological kathode only (in the majority of cases) at and during closure of the exciting current, at the physiological anode only, at and subsequently to break of the current.* A remarkable exception in localisation of electrical excitation is however shown to exist in many, perhaps

most, protozoans, where the excitation is indeed conspicuously polar, but appears at closure to be localised at the anode, on opening the current at the kathode; and Roux's observations upon the morphological "polarisation" of ova also fall under this category. Further, in many cases an equally marked *inhibitory* action of the current is exhibited in corresponding changes of form, which appear simultaneously with the manifestations of excitation, but are localised at the opposite pole. *Kathodic closure excitation* therefore implies a simultaneous *anodic closure inhibition*, *anodic break excitation*, *kathodic break inhibition*. Thus both the simultaneous polar effects, or after-effects, of current, and the subsequent effects at the same pole, as a rule, exhibit an antagonism (as is more particularly expressed in the opposite reactions of "electrotonic" changes of excitability at the physiological poles) by which it is possible to demonstrate the inhibitory effects even in such cases where, failing a tonic state of excitation, no visible alteration of form appears. So far as may be concluded from experiments on muscle, the current, provided its strength does not exceed certain limits, appears to traverse the intrapolar area without producing any perceptible alterations within it. Under some conditions excitation phenomena appear in the vicinity of the physiological pole during closure of the anode and after opening the kathode; but these seem to be due to diffusion of current and formation of secondary electrode points, and are accompanied by simultaneous, antagonistic changes (inhibition) in the region of the other pole.

The persistence of the excitatory or inhibitory effect of current during closure, as well as the localisation and antagonism at the poles, prove incontestably that *the consequences of electrical excitation are only a special manifestation of commencing electrolysis in the living substance*. On this assumption it becomes intelligible that the anodic and kathodic alterations should neutralise each other when produced by a transverse current at the opposite longitudinal margins of a muscle-fibril, or any minute tract of contractile substance (*e.g.* a pseudopodium). This view is not contradicted by the fact that in certain kinds of protoplasm the changes which underlie the excitation appear to be localised not at the kathode, but conversely at the anode; for this is obviously dependent on the quality of the excitable substance, which is not necessarily the same in all cases. These brief observations

must suffice for the present. The subject will be taken up again in connection with the theory of electrical excitation, in so far as it is possible to formulate any such propositions.

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CHAPTER IV

ELECTROMOTIVE ACTION IN MUSCLE

THE potential energy stored as chemical force in muscle, as in all other living tissue, yields in general three forms of vital energy, i.e. mechanical work (mass motion) and molecular motion in heat and electricity. In so far as muscle-cells proper are concerned it is the first of these which plays the weightiest part, and must be regarded as their characteristic function. The production of heat is not nearly as conspicuous in comparison, although in warm-blooded animals it also plays an important part in the economy of the organism. Finally, the development of electricity, which alone concerns us in the present connection, falls, with a few negligible exceptions, so far behind the other two forms of living energy that the most refined methods and delicate instruments are needed in order even to ascertain its existence. That, notwithstanding such disadvantages, this chapter of electro-physiology should be among the best known and most carefully worked out in Physiology is mainly due to the fact that since the discovery of the marvellous action of the electrical current upon excitable parts of the body, and the epoch-making controversy between Galvani and Volta, the idea that the mysterious phenomena of muscular and nervous activity were in some degree related to the no less obscure force of electricity never wholly vanished. Although the conviction subsequently obtained that the force which travels from nerve to muscle (the "nervous principle") is not in itself electricity, the rapid additions to the theory of electromotive action in certain animal tissues, and in muscle and nerve in particular, kept alive the presumption that these manifestations cannot be without import for the function of the parts in which they are exhibited.

Soon, however, in spite of innumerable labours and discoveries in this well-worked field, a marked contradiction asserted itself between the sum of theoretical and experimental data, and the almost total ignorance of their significance for the function of the tissues involved: here we are not yet emancipated from the stage of more or less well-founded conjecture. In striking contrast, on the other hand, is the electrical development in the living organs of those wonderful fishes, armed with powerful batteries, which afford a solitary illustration of the manner in which from insignificant beginnings in muscle or gland cells, where the electromotive action is hard to demonstrate, organs have been developed whose function as powerful electrical weapons of attack and protection is unmistakably attested. The importance of these facts cannot be neglected, and the interest manifested in the department of electro-physiology now before us is the more legitimate, since the fundamental researches of Matteucci, du Bois-Reymond, L. Hermann, and others provide a basis which is not merely a satisfactory starting-point for future labours, but from exactness of method guarantees the true interpretation of all such observations. Notwithstanding the importance which attaches to the historical development of the subject, it cannot be entered on here, and indeed could only be abbreviated from the masterly review given by du Bois-Reymond in his classical "*Untersuchungen*."

We shall therefore proceed at once to the description of electromotive action in the "resting" muscle.

I.—CURRENT OF REST IN MUSCLE

Between 1840-1843 it was discovered almost simultaneously by C. Matteucci and E. du Bois-Reymond that isolated, striated muscle, under certain conditions, exhibited pronounced and regular electromotive activity. This opened up a vast field of electro-physiology, the further investigation of which will always stand out as an admirable achievement of du Bois-Reymond, after whom Hermann has made the greatest contributions. If a long strip is cut out of the middle of a frog's muscle with parallel fibres and regular structure (e.g. sartorius, gracilis, semimembranosus), a so-called muscle-prism, or muscle cylinder, is obtained, where two end-surfaces are formed by

artificial cross-sections, while the upper surface (the "natural longitudinal section" of du Bois) corresponds with the natural, uninjured surface of the muscle. If unpolarisable electrodes are so applied to the muscle-prism that the one leads off from the artificial cross-section, the other from the middle of the natural longitudinal section, it will be found, with a properly sensitive galvanometer in the circuit, that there is invariably a pronounced deflection, *i.e.* a current, which flows in the leading-off circuit from longitudinal to transverse section, in the muscle on the contrary from cross-section to longitudinal surface.

Since any point of the longitudinal section, when connected with any point of the transverse section, invariably gives a current in the same direction, it may be stated generally that the entire surface of the muscle cylinder is positive, and every cross-section of the same negative in potential. It soon appears, however, that the distribution of potential is unequal; if the muscle cylinder is conceived as divided in two halves, by a plane parallel with its ends, and passing through the centre, the greatest positive potential at the surface corresponds with the "equator," *i.e.* the circumference of this section. From the equator the positive potential on either side declines unequally, *i.e.* falls more rapidly towards the end-surfaces, until at the margin between longitudinal and transverse section it becomes practically zero. Every line of potential, or isoelectric curve, therefore, forms a circle parallel with the equator. The negative potential always decreases at the ends, on either side, from centre to periphery. It is easy to see from this distribution of potential that the magnitude of decline may vary considerably, according to the position of the electrodes of the leading-off circuit, so that the lines of current can fall into a strong, weak, or ineffective arrangement. There will obviously be no current on leading off from two points of the equator, or any isoelectric curve parallel with it; nor from points of the longitudinal section symmetrical with the equator, or corresponding points of the terminal sections. On the other hand, a weak variation appears on leading off from two points of the longitudinal section asymmetrical with the equator, or two asymmetrical points of the section itself, or from both artificial cross-sections. Fig. 102 gives a schematic representation of all these possible cases; *a, b, c, d* stand for sections of the muscle cylinder; the arrows show the direction of current flowing into

the leading-off circuit. There is practically no current in the circuit uniting symmetrical points.

If the potential at each point of a longitudinal section is expressed by an ordinate, falling upon the longitudinal section as

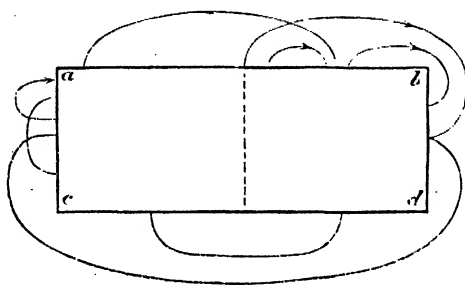


FIG. 102.

abscissa, the line which unites the summits of the ordinates will, in consequence of the rapid decline of potential towards the end-surfaces, be a curved line with a sharp drop at either extremity. A similar effect is produced at the cross-section (Fig. 103).

If the regular muscle cylinder is shortened by making new sections, cylinders (prisms) will result, which follow the same law of the muscle current; the muscle can further be split up longi-

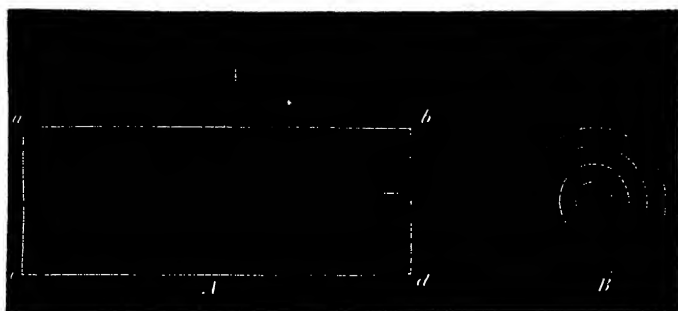


FIG. 103.—Distribution of potential in straight muscle cylinder. (Rosenthal.)

tudinally, parallel with the fibres, so that, as du Bois expresses it, an artificial longitudinal section is formed which, like the natural surface, is positive to the transverse section. And no doubt if it were possible to investigate *a single primitive fibre* in itself, the same opposition would still obtain between longitudinal section

and transverse section. Indeed, there is some justification for the further postulate of electromotive activity in the same sense in each fraction of a primitive fibre. Thus du Bois-Reymond arrived at the conclusion that each muscle-fibre was composed of minute electromotive particles ("molecules") suspended in a conducting fluid, and he developed on this basis a theory of the electrical phenomena in animal tissues, which long held the field undisputed. It was a necessary corollary of this view to suppose—as seemed to be supported by experiment—that uninjured, striated muscle with a natural transverse section gave exactly the same electromotive reaction as that furnished with an artificial cross-section. By "natural transverse sections" du Bois-Reymond understands the total of the uninjured ends of muscular fibres still normally connected with the tendon. This theory of the electromotive equivalence of artificial and natural cross-sections rests mainly upon the electromotive reaction of the apparently uninjured frog's gastrocnemius, and the complicated structure and general application of this muscle make it advisable to examine more closely into the much-discussed "gastrocnemius current." Leaving out for the moment the fact that the really uninjured muscle gives no electromotive reaction (*infra*), it may be assumed that the achilles tendon is, as in the majority of cases where no special precautions are taken, negative towards the remaining surface of the muscle. Owing to the complex structure, the distribution of surface potential will then be far more elaborate than in a muscle cylinder with regular parallel fibres. Rosenthal (2) gives a very comprehensive description of the structure.

"Two plates of tendon, above and below, are joined by muscle-fibres running obliquely between them, so as to form a semiplumiform muscle. Now let the upper tendon-plate be folded in the middle, like a sheet of paper, and the two halves grown together. There is thus an upper plate of tendon lying inside the muscle, with muscle-fibres starting obliquely from it on either side; the lower tendon is, however, curved through the folding together of the upper, so that the whole muscle assumes the form of a root, cleft longitudinally; its smooth surface (which faces the bone of the shank) consists entirely of muscle-fibres, and exhibits only a fine longitudinal streak as indication of the tendon concealed within, while the bulging dorsal

aspect is covered in its lower two-thirds by tendon-substance, continued below into the tendo achilles" (Fig. 104).

The gastrocnemius is therefore provided by nature with an oblique transverse, and a natural longitudinal section, which

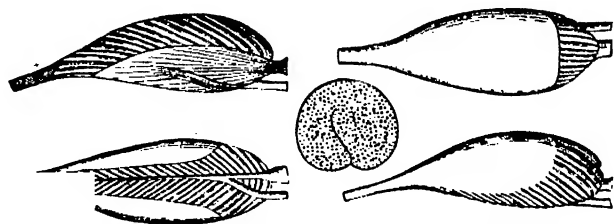


FIG. 104.—Schema of Gastrocnemius structure. (Du Bois-Reymond.)

include the whole of the flat, and a small part of the bulging surface. This is in correspondence with the characteristic distribution of potential on the surface of the muscle. If a regular muscle cylinder is twisted obliquely (Fig. 105) so that the terminal cross-sections run parallel with each other, but obliquely with the axis, the curve of greatest positive potential corresponds, not with the equally oblique, centrally placed, elliptical equator, but with a winding curve drawn towards the blunt corners. Conversely, the negative potential is greater at the sharp, than at



FIG. 105.—Distribution of potential in oblique muscle cylinder. (Booth.)

the blunt, corners of the cross-section. When there is no current through the regular muscle cylinder, so that the contacts of the leading-off circuit are equidistant from the geometrical equator, it is evident that a current will be obtained, flowing in the muscle from sharp to blunt edge (du Bois' "Neigungstrom"). Such

currents are exhibited by the gastrocnemius provided *ab initio* with an oblique section. A strong current is effectually obtained on leading off from the upper and lower ends of the muscle, flowing in the muscle itself in an ascending direction. But currents of greater or less strength appear with almost any lead-off, since equipotential points are rare upon the surface.

If the ascending gastrocnemius current is not too weak it may easily—like all longitudinal currents—be demonstrated with the “physiological rheoscope” (rheoscopic leg), and this not merely in the experiment of Galvani and Volta as “contraction without metals,” in which the sciatic nerve drops upon the convex surface of the muscle, and causes an external short-circuiting of the current through the nerve, but also by including the nerve in a circuit of low resistance led off from longitudinal and transverse section. In this way a twitch is obtained from the leg on closing, and subsequently on opening, the circuit. While at the time of the famous dispute between Galvani and Volta, it was the excitation of a motor nerve through the muscle current, in the form of “contraction without metals,” that excited the greatest interest, since the experiment appeared to be a direct proof of the existence of an electricity peculiar to the animal tissues, the interest in this point subsequently disappeared when it was no longer disputed. On the other hand, another attempt to demonstrate the muscle current by a physiological method, deserves more attention. If the current of the longitudinal section suffices to excite the nerves of a rheoscopic leg, it is conceivable that the muscle itself may be excited by its own current, or current from another muscle (Hering, 4).

As early as 1859 Kühne (3) described a characteristic reaction in the transversely divided frog's sartorius, appearing when the cut surface was dipped into various fluids, and ascribed by him to *chemical* excitation of the exposed fibres. If the vertically dependent, curarised muscle is brought into contact with a watch-glass of 0.6 % NaCl, immediately after making a section, a twitch almost invariably follows at the moment of contact between cut surface and fluid. The muscle is thus jerked out of the fluid, but on relaxing it dips in again, when a second twitch follows, and so on. In this manner a long series of rhythmical contractions (over 100) may be discharged. The experiment comes off with a number of other fluids. Besides

different concentrations of NaCl solution, Kühne found that solutions of fixed alkalis and mineral acids up to 0.1 % were very effective, as well as solutions of different salts, but he failed to detect a twitch when the section was brought into contact with distilled water, alcohol, creosote, concentrated glycerin, and syrupy lactic acid; Wundt and Schelske further noted that concentrated solutions of sublimate produce no twitch from the transverse section. Kühne held that (*supra*) all cases in which he observed twitches, on touching a fresh section with fluid, were due to *chemical* excitation of the exposed fibres. But this is a doubtful hypothesis in view of the fact that with 0.5–0.6 % NaCl solution, which is well known to be comparatively harmless, the effects in question appear peculiarly well marked and persistent. It is, moreover, remarkable that salt solution when applied to the muscle section that has been moistened, does not produce any permanent excitation, as would be the case if the fluid acted as a chemical stimulus. And it may be shown that the excitatory effect fails if the solution is applied to the transverse section only, and hardly, if at all, to the longitudinal surface of the muscle. Hering (4) produced this, *inter alia*, by placing a small strip of greased paper round the cross-section of the muscle, so that its lower margin coincided with the margin of the section. A muscle prepared in this way does not twitch on bringing the transverse section into contact with the salt solution, as must inevitably occur if it was a *chemical* excitation. "If, on the other hand, the muscle is dipped into the fluid above the strip, the twitch reappears again." Accordingly if the experiment is to succeed "it is essential that there should be on the one hand a connection between the transverse section and the lowest part of the longitudinal surface, while on the other this conductor must not have too great a resistance, *i.e.* the quantity of NaCl solution which produces it must not be insufficient." If then—as can hardly be doubted from the above—this is an *electrical* excitation of the muscle, by sudden short-circuiting of its own current within the wall of fluid that rises at the moment of contact, from transverse to longitudinal section, it is easy to understand that all non-conducting, or ill-conducting fluids, as we learn from experiment, are ineffective, even if they have a demonstrable chemical action on the substance of muscle (sublimate, alcohol, water). Indeed, as Hering pointed out, the mere reaction of the muscle on

touching its cross-section with a fluid is a tolerably sure indication as to whether such a fluid is a good or bad conductor. Upon this assumption we may explain other easily verified experiments, which to some degree are mere modifications of the fundamental experiment quoted. If a drop of salt solution is allowed to fall upon a cut at right angles to the direction of the fibres in a muscle, the cut ends usually twitch, and the wound gapes open. Again a twitch can be provoked from the transversely cut sartorius if the longitudinal and transverse sections are connected by a moist conductor (*e.g.* strip of liver, dead muscle, etc.) The preparation can also be laid upon unpolarisable zinc trough electrodes with mercury closure, leading off from the fresh transverse section and a point of the longitudinal section adjacent to it. Again, if the cross-section of a freely dependent sartorius is brought into contact with the longitudinal surface by bending the end with a glass rod, the muscle will twitch from the sudden closure of its own current. Finally, Hering succeeded in producing a twitch in an uninjured, by current from an injured, muscle. To this end the uninjured sartorius was fixed by the bones so as to hang down in a slack curve. The second vertical muscle was then brought into contact with it, the cross-section being applied to the surface of the first muscle. "When both muscles are very excitable they may both twitch; for as, on contact with the cross-section, it is very likely that part of the longitudinal surface also will be in contact with the uninjured muscle, closure of current in the injured muscle is effected by the uninjured, and both are simultaneously excited." This always occurs, indeed, if the cut end is bent over. In all these experiments short-circuiting of the muscle current is effected by *moist* conductors. *Metals* indeed are of very little use on account of their extraordinarily rapid polarisation, though at first sight the contrary might be expected. Hering, like Kühne (5), found little or no twitch, when contact was formed at the fresh cross-section of a curarised sartorius by a platinum plate, while a wire of the same metal, connected with a mercury key, effected contact at different points of the conducting surface.

The fact that current from the longitudinal muscle section may under certain conditions excite not only the nerve of a rheoscopic leg, but also the injured muscle itself, or even one that is uninjured, gives *a priori* reason to suppose that the same factor plays a part in all electrical excitation of injured,

i.e. electromotive, muscle, and it is the more essential to bear in mind these phenomena of *interference between the artificial and the natural current*, since they involve facts which have led to important theoretical conclusions.

We have already cited, as a cogent proof of the validity of the law of polar excitation, the characteristic response of a muscle with parallel fibres, injured at one end only, to longitudinal passage of current; as seen, *e.g.*, in the fact that the excitatory effect of closure or opening of a current is invariably diminished or abolished, when it leaves or enters by the demarcation surface. Since in the former case the direction of that fraction of the muscle current which branches into the exciting circuit is always opposed in direction to the battery current, the latter is necessarily weakened by the former, and the question arises whether this in itself would not be sufficient to account for the diminished excitation at closure of the circuit. Obviously in this case, if the muscles are introduced into the same circuit, one behind the other, one of them being injured at one end, the closure of the current would affect both muscles equally, *i.e.* the make excitation with admortal direction of current would be abolished or lessened, not merely in the muscle with an artificial cross-section, but in the normal preparation also. Yet this is not the case, and the theory is no less definitely refuted by the fact that the death of the fibres *at both ends* of a muscle with parallel fibres, produces the same depression, or abolition, of excitability towards the closure of ascending as of descending currents. On the other hand, it appears as if the augmented effect which is often to be seen at closure of weak "abterminal" battery currents after injury to one end of the sartorius, is essentially caused by the deriving current from the muscle superadded in this case, algebraically, to the exciting current.

Under certain conditions, to be discussed below, a spurious break twitch appears in consequence of interference between the demarcation current and an artificial excitation current, which might easily be taken for the effect of a real break excitation, and is in fact frequently confused with it. Given a leading-in circuit of comparatively low resistance, so connected with a curarised sartorius provided at the pelvic end with an artificial cross-section, that the unpolarisable contacts are applied, on the

one side to the cross-section (or bones of the pelvis leading off from it), on the other side to the tibial end of the tendon (or tibia itself); then at the moment of closing the circuit, which has been broken at any point, the longitudinal current will equalise itself, and will presumably, on leaving the normal muscular substance at the small end of the muscle, discharge a make twitch, if the intensity of the shunt current is sufficient, the resistance in the circuit being as low as possible—conditions which are scarcely afforded in the case before us. But if we suppose for a moment that we are really dealing in this case with discharge of a make twitch of the muscle through short-circuiting of its own current, a twitch that was referable to this cause would also be produced if the fraction of the muscle current shunted off was compensated, or even over-compensated, by a galvanic current sent through the intrapolar tract, *i.e.* the entire muscle, in an ascending direction—finding closure again suddenly at the instant the battery current is broken. In the case in which compensation is complete, and unavoidable secondary effects of the compensating current negligible, the excitation effect will be as great on opening the galvanic current as on the previous closure of the circuit. The experiment is sure to be successful, if the resistance in the leading-off circuit is reduced as much as possible by shortening the intrapolar tract of the muscle (6).

It is often sufficient to use the lower half of the sartorius only, by killing a segment in the middle of the muscle with heat (artificial thermic section), fastening this point with small needles to a cork plate, and leaving the lower third of the muscle free, weighted only by the dependent tibia. Two unpolarisable electrodes, one of which is placed upon the upper margin of the tract destroyed, while the other (near the tibia) dips into a vessel with concentrated salt solution, serve on the one hand to lead off the muscle current, and on the other to lead in the compensating battery current from a Daniell cell. In order to graduate the intensity of the latter, a rheochord is introduced into the circuit, which serves as a deriving circuit to the muscle. Provision should be made for opening the circuit at two different points, since the object is to investigate the difference in excitation effect on breaking the main current with simultaneous short-circuiting of the muscle current, and on

simply cutting out the former. For this purpose two mercury keys are introduced into the circuit, one between the cell and the rheochord, the other between the latter and the muscle. The former is denoted below as the key in the principal circuit, the latter as key in the deriving circuit. If the key of this deriving circuit is closed immediately after the thermic section has been effected, the key of the primary circuit remaining open, a perfectly visible, though usually weak, closure twitch is seen under favourable conditions in very excitable preparations. The results are more certain if the unpolarisable electrodes are placed near together, in direct lateral contact with two points of the surface of the muscle, whereby the resistance in the circuit can be suitably reduced. If the upper half of the uninjured sartorius is stretched on a cork plate, and one electrode placed at the pelvic end, the other at a slightly lower point of the longitudinal surface, then on leading a weak or medium current, descending or ascending, through the muscle, a twitch occurs at every closure, while on opening the circuit by the principal, or shunt key, no trace of change of form in the muscle is apparent. The result of the experiment is very different when an artificial (thermic) section has previously been made at the pelvic end of the muscle; if the negative electrode is now in contact with the heat-rigored end of the muscle, while the positive electrode is applied to the nearest point of the uninjured surface, there is, with rare exceptions, in excitable preparations, immediately after the injury, a distinct twitch, the index of excitation in the freely-depending half of the muscle, as soon as the deriving circuit is closed—the principal circuit remaining open. It is obvious from the conditions of the experiment that this also is an excitation resulting from the passage of the muscle current through the shunt current. Whether this happens or not, there is invariably, under these experimental conditions, a pronounced shortening of the muscle when a weak battery current opposed in direction to the muscle current (*i.e.* in this case ascending) is made for a short time and broken in the principal circuit. Since the physiological kathode is at the seat of injury, the make excitation either fails altogether, or is very insignificant. This result, however (given a sufficient distance of the leading-off, or leading-in, electrodes), appears at the opening of the principal circuit only, while there is no sign of mechanical change on

opening the deriving circuit. A maximum difference of electrical potential in the points of the muscle, from which the electrodes lead off, as well as lead in, is the only indispensable condition. In view of the preceding discussion, there can be no doubt that the striking difference of effect on breaking the circuit at two different points, is solely due to the fact that the demarcation current in the one case finds an external circuit of comparatively low resistance on opening the battery current, which is wanting in the other case. The twitch, though coincident in time with the moment of breaking the circuit, cannot be regarded as a true opening twitch due to internal reaction of the muscle, but is much rather a closure twitch, discharged by external short-circuiting of the muscle current (Biedermann, 6).

If the distance between the two electrodes is very small, there will, as a rule, even with minimal currents, be hardly any perceptible difference in the magnitude of the break twitches, whether the battery circuit or the muscle circuit is opened. Intermediate electrode points may be found, in which there is a certain difference in the magnitude of twitch, according as it is discharged at break of the principal, or deriving, circuit, since in the latter case it decreases in proportion as the point of entrance of the atterminal battery current recedes from the limit of the thermic section, the kathodic contact at the cross-section remaining unaltered. This is easily explained in view of the pronounced internal short-circuiting of the muscle current that always occurs in the immediate vicinity of the electromotive surface. For if countless lines of current pass out at the surface, in parts that are still excitable, near each transverse section of each single primitive fibre, and thus of the entire muscle, a battery current entering at this region of internal short-circuiting must *ipso facto* compensate a portion of these lines of current, some completely, some imperfectly, while others again may be over-compensated. This, however, implies that those spots more or less entirely lose their character as kathodic points of the muscle current, or even become anodic points of the battery current. If the latter is opened again, the former condition is instantly recovered; the points once more become kathodic points of the muscle current, and are excited by it. The battery current therefore abolishes in part the internal closure

of the muscle current, the sudden restoration of which, at break of the battery current, produces a make contraction.

It is indeed a matter of indifference whether the break of the galvanic current occurs in the muscle or battery circuit; in the latter case it must be taken into consideration that the branch of the muscle current, which is closed by the rheochord, and compensated, or over-compensated, during the passage of the galvanic current, finds its closure at the moment the latter is broken, and hence induces the "spurious break twitch." The theoretical differences in magnitude of twitch in either case are not, however, perceptible, because the contractions are very marked in both cases.

Since the last-named effects of excitation are of importance in regard to certain facts respecting electrical excitation of nerve, to be described below, we must consider them a little more in detail. If a loop of moist thread is laid round the muscle—stretched, to obtain a graphic record of its twitches, in Hering's double myograph—so that the current enters anywhere in its continuity, in the close vicinity of an artificial section produced by crushing, while it leaves it again at the pelvic bone, pronounced break contractions, which are almost entirely independent of the length of closure, may be seen directly a weak current is sent in, without regard to the point at which the circuit is opened. If, while the kathode remains *in situ* at the uninjured pelvic end of the sartorius, the physiological continuity of the muscle is interrupted somewhere near the middle by crushing with forceps, the thread being applied now to one side, and now to the other, of the seat of injury, but always close to its margin, break contractions may be seen in both cases at equal current intensity, in one of the halves divided by the injury, the contraction being always in that half where current enters at the artificial section. If the electrode by which current enters is removed ever so little from the point of injury, the effects of excitation being tested at each new position, it may be seen that the "spurious break twitches" as a rule become weaker, even at points of the normal longitudinal surface that are no more than 2 mm. from the part injured, and disappear altogether as soon as the thread is moved still further, provided closure is effected by the key of the deriving circuit.

If we are justified in saying that the only fact of importance

in the discharge of spurious break twitches by internal shunting of the demarcation current, is that the kathodic points of fibres in immediate juxtaposition with the electromotive surface, by which current leaves the muscle, become temporarily the points of entrance of an adequate galvanic current (in which case there will only be partial compensation of the demarcation current), it might be expected that spurious break twitches would appear, not only—as in the case described above—on applying “atterminal” battery currents, but also when, on “abterminal” passage of current through the entire muscle or a portion of the same, the entry of the current occurs at the limit of an artificial cross-section in the region where the muscle current leaves it. It is in fact sufficient, for the discharge of spurious break twitches of great vigour, to make an artificial section at the pelvic end of a sartorius, followed immediately by a weak descending galvanic current through the entire muscle, entering laterally close under the margin of dead and living substance by means of a thread electrode.

If further, with abterminal direction of current, the dead ends of fibres are conceived as connected by any kind of conductor with the zone of normal longitudinal muscle-surface impinging on the border, we might expect spurious opening effects of excitation in this case also. Such, *e.g.*, do appear when one end of the muscle is crushed with small forceps; the bulging and curving of the longitudinal surface of the fibres then give repeated opportunities to both muscle current and battery current to enter and leave at points in the uninjured surface of the muscle, and thus to discharge effective make, or spurious break, excitations. If, after ascertaining that an ascending current of medium intensity discharges no perceptible break excitation in a sartorius stretched in the double myograph, the muscle is crushed, as indicated, close to the lower end of the tendon, opening twitches will appear almost uniformly—direction, intensity, and duration of closure of the exciting current remaining constant—and must, according to the above, be regarded as *spurious* (Biedermann, 6; Engelmann, 7).

From this digression we may return to the consideration of the “current of rest” in muscle, its properties and its origin. Since, provided the galvanometer swings are not excessive, the deflections are known to be proportional to the intensity of the

current, it is of course easy to measure the intensity of the muscle current; yet, in view of the great and very variable resistance of vegetable and animal tissues, such measurements are on the whole of little value. Much greater importance attaches on the other hand to exact *measurements of electromotive force*. If two points of different potential are connected by a leading-off circuit to a conductor which is the seat of electromotive force, a branch of the current will flow through these, of intensity directly proportional with the E.M.F. which may be conceived as acting at the points of junction. The magnitude of the latter may thus be measured from the difference in potential between two points led off, and where it is possible to determine this exactly, it is also possible to determine the magnitude of the electromotive force. And the E.M.F. of the longitudinal current could be ascertained simply by measuring the P.D. between natural longitudinal surface and artificial cross-section. The difference of potential between two points is easy to determine experimentally, by a method invented by Poggendorff, and essentially improved by du Bois-Reymond (8).

FIG. 106.—Measurement of E.M.F. by compensation. (Du Bois-Reymond.)

The principle of the method is to replace the magnet from its deflected position to its original position of rest, by means of a fraction of the current of a standard cell, opposing and cancelling the original current. The known variable P.D. is thus a measure for the magnitude of the unknown difference to be determined. Such a "compensating" current can easily be derived from a measuring circuit by means of a rheochord, termed in this case a "compensator." If a constant current (K) is led through a straight or circular wire (Fig. 106 *a, b*), a definite "electrical fall" occurs in the circuit, since there are differences of potential at different points. Now, if the longitudinal section of a muscle (M), lying upon unpolarisable electrodes, is connected by means of a reverser (C) with the end (a) of the compensator

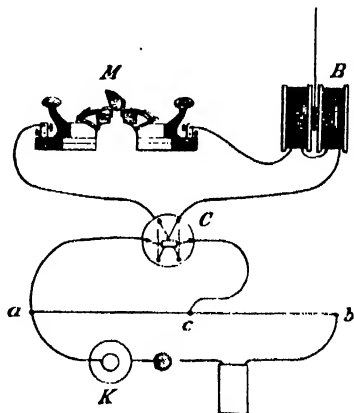


FIG. 106.—Measurement of E.M.F. by compensation. (Du Bois-Reymond.)

wire, while the point led off on the longitudinal section is connected with a metal slider (*c*) leading to the wire of the rheochord, the galvanometer (*B*) will be affected on the one hand by the difference of potential between the rheochord points *a* and *c*, on the other by that between the transverse and longitudinal surfaces of the muscle. It is easy at any moment by moving the slider (*c*) to compensate the deflection produced by the muscle current. The P.D. between longitudinal and transverse section of the muscle will then obviously be the P.D. between the points *a* and *c* of the rheochord wire. And in the

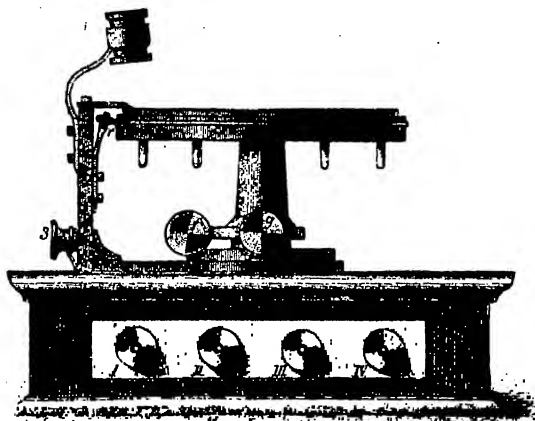


FIG. 107a.—Round Compensator. (Du Bois-Reymond.)

latter each millimeter corresponds with a given fraction of the E.M.F. of a Daniell cell.

In order to carry out these measurements quickly and conveniently, du Bois-Reymond constructed the "round compensator," in which the rheochord wire *a*, *b* is attached to a circular disc of ebonite. Its terminals are connected with screws I. and II.; from I. a wire also goes to IV., III. being connected with the metal pulley (*r*), which slides upon the rheochord wire, so that a given length of it can be included by moving the slider (Fig. 107 *a*, *b*).

By this method du Bois-Reymond took numerous measurements of the electromotive force between longitudinal and transverse sections of striated frog's muscle. The average was 0.035–0.075 Dan. According to Matteucci, the muscle-

current is stronger in proportion as the animal is higher in the scale, but it is difficult to get exact measurements of E.M.F. in warm-blooded muscles, on account of the rapid death of the tissue. That the muscle current is essential to the preservation of normal vital activities in the muscle appears directly from the fact that dead muscle has no electromotive action, or at most exhibits excessively irregular and weak reactions. Moreover, the E.M.F. of the excised muscle, provided with a cross-section, undergoes, as du Bois pointed out, a slow decline; the process of death, creeping slowly from the cut surface, gradually involves all the injured fibres of a muscle, so that they become rigid and incapable of electromotive action. Accordingly, the limit between dead fibres (confined at first to the cut surface) and the living part of the contractile substance (*"the demarcation surface"*) encroaches inwards in the course of the rigor.

We have frequently used the term "artificial section," even when there was no real cut surface, but only a demarcation surface as above. As a matter of fact each dead bit of muscle-fibre behaves as an indifferent tag (comparable with the tendon substance), which leads off from the artificial cross-section, *i.e.* limit between dead and living fibres. In this sense, therefore, it is quite legitimate to speak of a mechanical, thermic, or chemical section. As a general rule, moreover, the strength of the electromotive action is independent of the kind of death, or destruction, of a tract of fibres, so long as the process is actually accomplished.

If these experiments prove beyond doubt that the muscle

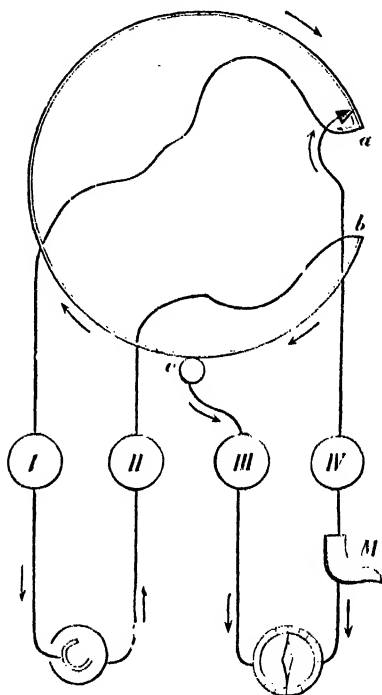


FIG. 107b.

current is a property of *living* tissues, it would still only appeal to us as a vital phenomenon of the first interest if it could be proved that du Bois-Reymond's law of the equivalence of natural and artificial sections was universally valid, *i.e.* that a P.D. between the tendon end and remaining surface of the muscle, corresponding with the muscle current, is demonstrable in all cases; in other words, if the "*pre-existence*" of the muscle current in intact living animals were a proved conclusion. But this, as we shall see, is by no means the case; on the contrary, the result of the innumerable experiments of a later date has been more and more in favour of the view upheld by Hermann, to the effect that the muscle current is not pre-existent, but is an artificial effect of the preparation. Matteucci long ago maintained that there was no trace of a muscle current in the uninjured living animal. According to him the current arises from the leading-off contacts. Du Bois-Reymond, who (*supra*) adopted the theory of a constant difference in potential between the achilles tendon (natural section) and uninjured surface of the muscle, chiefly on account of his first experiments with the frog's gastrocnemius, was subsequently obliged to modify his opinion. The starting-point of these last investigations of du Bois-Reymond was a series of observations on the effect of cold on the muscle current, which, as Matteucci had pointed out, produces a marked diminution. Du Bois-Reymond upon the whole confirmed Matteucci's conclusions as to decreased action in the muscles of cooled frogs. Gastrocnemii (which, on leading off from tendon and natural longitudinal section, invariably gave, according to du Bois-Reymond's original theory, a vigorous normal current) exhibited negative or reversed effects in the sense of a descending muscle current, while directly an artificial cross-section was provided they yielded an ascending current. Du Bois-Reymond designated the state of muscle induced, as he thought, by cold, the "parelectronic" state (*παρὰ νόμος* = against the law), because it gives no electromotive response, or even reacts in the opposite direction. The fact that these parelectronic muscles resume their "normal" activity from the moment they are laid upon pads of salt clay coated with an albuminous membrane, is due, however, less to warming than to the slow chemical alteration (corrosion) of the tendon, which is in contact with the concentrated salt solution of the leading-off electrodes and the albumen of the membrane. These fluids

gradually induce the same effect that is suddenly brought about when a mechanical or thermic section is applied by any method. Hermann (9) showed later, by conclusive experiments, that the E.M.F. of excised muscles does sink considerably through cooling, and rises again on increasing the temperature; according to Hermann the variation may rise to 22 % within the range of vital temperature, but is probably still greater, since, in the methods used, the deeper layers may not be affected in the same degree as the more superficial.

If in preparing, as well as in leading off from the muscle, care is taken to avoid all possible injury (especially at the tendon end), the electromotive effect is either negative, or the P.D. between surface and natural section is so negligible that it might legitimately be ascribed to inevitable disturbances from exposure. Moistening the natural section with fluids which do not attack the muscle-substance chemically, *e.g.* physiological NaCl solution, gives no perceptible development of current. Later on in du Bois-Reymond's investigations, it appeared that the supposed effect of cooling is not so important in the development of parelectronomy, but that all muscles are, rather, permanently at a more or less pronounced grade of the parelectronomic condition. This state is not therefore abnormal and an effect of cooling, but is perfectly normal and regular. As Hermann remarks, the term "parelectronomic" might with more justice be applied to the state in which current is fully developed between end of tendon and muscle, than to that which du Bois-Reymond designates by it.

Du Bois-Reymond's explanation of the parelectronomic state will be discussed below. Here it can only be said that he attributes the failure, or absence, of current between surface and natural section to the presence of a thin layer of specific muscle-substance at the natural section, which by its contrary action partly compensates, or even over-compensates (*i.e.* abolishes), the normal electromotive action of the remaining mass of the muscle.

The production of current when the natural cross-section is moistened with concentrated NaCl solution, acids, or alkalis, or is cut or heated, must accordingly be referred to the chemical, thermic, or mechanical disturbance of this thin sheet, called by du Bois-Reymond the parelectronomic layer. This theory of a parelectronomic condition at various stages of development

affords a simple explanation of the vigorous, normal current of the apparently uninjured gastrocnemius, as also of the irregular effects which may be produced on leading off from tendon and natural longitudinal section of the different thigh muscles. But it is evident that, under the given conditions, the state of *no current* must be regarded as normal. If it could be proved that all muscles in the perfectly uninjured state are invariably, and under all conditions, currentless, the hypothesis of a special layer working in a contrary direction at the natural section would obviously be superfluous. The entire controversy as to the pre-existence of the muscle current turns, therefore, as Hermann said, upon whether it can be demonstrated before the animal is skinned, on the muscle *in situ*, with normal circulation. This might seem comparatively easy on the frog, since its moist, thin skin lies loosely on the muscles, and forms a relatively effective sheath. And it is in fact the most favourable object for the experiment. Du Bois-Reymond devoted much time and trouble to the investigation of the muscle current in the living, uninjured frog with intact skin, and concluded, finally, that normal differences of potential did exist in the sense indicated. Nevertheless, this also appeared later to be an interpretation against which serious objections can be urged. In leading off from frogs, and frogs' limbs, with intact skin, du Bois-Reymond again employed trough electrodes, filled with concentrated NaCl, and covered with an "albumen membrane." It was soon found that the contact first applied was always positive to the second contact, so that after some time a current of low E.M.F. appeared, in the direction of the longitudinal current in a skinned frog. The first effect depends, as du Bois found, upon an electromotive force in the skin of the frog itself. It is here sufficient to state that the E.M.F. of the skin is vertical to its surface, current being directed from without inwards (of course reversed in the galvanometer circuit). Now since these strong natural effects are easily disturbed by moistening the outer surface of the skin with corrosive fluids, there must always be a current in the above sense when the skin is brought into unequal contact with the leading-off electrodes, since these are not perfectly indifferent, *i.e.* the less effective, or ineffective, point becomes positive to the other.

It might be expected that the *normal* current from the

muscles below the skin would appear unmistakably at the moment at which both leading-off points became electrically indifferent. This seemed in fact to be the case in du Bois' experiments, but the P.D., strictly speaking, was always very low, and gradually diminished. This last fact indicates that the parelectronomy of the subcutaneous muscles was abolished by the gradual permeation through the skin of the NaCl solution, so that we seem to be *a priori* justified in supposing that the very first signs of the normal muscle current are also due to corrosion of the natural transverse section. Hence, as Hermann (10) was the first to point out and demonstrate directly by corrosion with silver nitrate, which perceptibly alters (darkens) the subjacent muscles, this experiment cannot be held conclusive for the theory of the pre-existence of the muscle current. "If the points of corrosion are so chosen that there is no subjacent aponeurotic muscle-surface (*e.g.* the outermost points of the toes, and skin of back), there is actually no deflection corresponding with the muscle current, but the circuit is as free of current as is possible in any circuit which contains moist conductors and metals." If creosote, silver nitrate, or still better, corrosive sublimate, are used on Hermann's plan, instead of the rapidly dissolving salt solution, it is really possible at a given time to demonstrate complete absence of current between the two principal contacts with the skin, while later on corrosion sets in, and a weak normal current is produced. In fishes, where the skin current is usually less strongly developed than in the frog, it is generally sufficient to keep them a certain time in water at the temperature of the room (Hermann) to produce absence of current on leading off from the immobilised uninjured animal. We have shown above, when describing the parelectronomic condition, that it is possible to obtain a completely isolated muscle which is absolutely currentless, and du Bois himself observed the same repeatedly on the frog's gastrocnemius. That, this notwithstanding, he should still maintain the pre-existence of muscle currents, was principally because, in so many other cases, the same muscle exhibits small but regular differences of potential in spite of every possible precaution. We must, however, accept Hermann's view that in such cases also the electromotive action depends on the unobserved entrance of injurious, *i.e.* chemically disturbing, fluids (skin-secretion, muscle juices, etc.), unequal rise of temperature, contact, or

pressure, which can only be avoided by complete familiarity with the deleterious matters on the one hand, and the extraordinary sensibility of the muscle-substance on the other. Above all, contact with any wound in the muscle, or the fluid by which this is moistened, must be carefully avoided. For, as was pointed out by du Bois-Reymond, the exposed fibres, dying or dead, *e.g.* in an artificial cross-section, are extremely active in developing current. These facts are very striking in regard to du Bois' *dictum* that only such matters as attack the muscle-substance chemically, and thereby, as he said, destroy the parelectronic layer, develop electromotive action, since we are justified in assuming that the muscle-substance itself does not undergo chemical alteration. But it must be remembered that the exposed fibres rapidly set up rigor, and undergo chemical changes, which of course develop acids. Since, on the other hand, it is known that even very dilute acids are highly injurious to the vital properties of muscle, it is natural to refer the current-developing property of the artificial cross-section to the acidifying of the muscle-substance. How far this assumption is really justifiable must be decided later.

The theory of pre-existence of electromotive action meets with special difficulties in the uninjured, or apparently uninjured, adductor group of the frog. In the majority of cases du Bois found a descending current between the two ends of tendon, but there were also cases of complete absence of current, as well as of a reversed current. The current between upper end of tendon and equator (du Bois' "upper current") was greater, as a rule, than that between equator and lower end of tendon ("lower current"). Yet du Bois also found the opposite, there being even cases in which both ends of tendon were positive to the equator. These discrepancies and confusions were, as Hermann points out, sufficient in themselves to shake the parelectronic theory; but such was not the case. On the contrary, on the ground of certain results with the adductor muscles it obtained a wider extension from the presumption of a parelectronic strip, developed in many cases in place of the parelectronic layer (11). By this du Bois-Reymond designated the (rare) case in which an artificial section in the neighbourhood of the end of the tendon is positive, and not, as usual, negative, to the longitudinal section. It will be shown later that all these irregularities admit of a simple explanation;

for the moment we can only say that the muscles of the frog's thigh, *e.g.* sartorius, may be obtained perfectly free from current without much difficulty (16). The proof that skeletal muscle can always be obtained free of current with proper precautions does not, however, exhaust the evidence against electromotive action in uninjured muscle. In 1874 Engelmann (12) pointed out that the heart is a muscle peculiarly well adapted to investigation in the normal, uninjured condition. Experimentally, indeed, with every variety of lead-off, it gives no current. It is, however, obvious that an artificial section of the heart must be as negative as that of any other muscle: and it was with knowledge of this that Matteucci constructed a battery of pigeons' hearts with transverse sections. It is interesting relatively to the theory of the longitudinal sectional current that (Engelmann, 12) the E.M.F. between the artificial transverse section and natural surface of cardiac muscle declines very rapidly. This is the more striking since it has long been known (as pointed out by du Bois) that the longitudinal current of monomeric skeletal muscle, when once developed, is singularly constant. Engelmann found, *e.g.*, that the E.M.F. in the sartorius in 1 hour fell to 81.1 %, in 24 hours to 43.6 %, and in 48 hours to 30.8 % (average of 45 experiments). Renewing the section, *i.e.* application of a fresh, deeper cross-section, is usually of little use, leading at most to a slight augmentation of the muscle current. In the heart the results are very different. Here refreshing the old section is sufficient to restore the E.M.F. to its original vigour. Hence it might appear as though the development of the paracellular layer could be directly observed in this case. The fact, however, is easily interpreted, considering the analogous behaviour of *polymeric skeletal muscle*. Two long muscles, divided into many short segments by tendinous intersections, run along the inner side of the body-wall of *Salpandra maculata*. If such a band-shaped muscle is excised, divided transversely through a single segment, and protected from drying, it will be found infallibly that after some time this injured segment alone shows symptoms of rigor, while the rest retain their normal appearance and excitability, *i.e.* mortification has been arrested at the nearest tendinous intersection. On leading off from such a muscle to the galvanometer, on the one side from an artificial cross-section, on the other from any point of the muscle surface, a normal current will of course

appear immediately after making the artificial section. According, however, to the pre-existence theory, this would still be demonstrable if the injured segment were completely rigored, since there would then be an unequal lead-off from the natural cross-section of the next segment, as in the tendon or bones of a monomeric muscle. But this is not the case; the longitudinal sectional current only lasts so long as a portion of the substance of the segment provided with an artificial cross-section is living; it becomes *nil* when this segment is completely rigored, and only recovers its former proportions when a new section is made on the farther side of the tendinous intersection.

Analogous relations exist in cardiac muscle. This stands apart from other striated muscle not only in regard to the complicated character of its fibres, which is here of no importance, but also with reference to the much smaller dimensions of its morphological elements, which consist of minute, microscopic cells. Engelmann showed that the single cells of cardiac muscle proved themselves in dying to be perfectly separate individuals, exactly resembling the single constituents of polymerous muscle. The process of rigor induced by section originates in the heart at a very short distance from the wound, and therefore occurs more quickly than in normal muscles with long fibres, so that here, as in polymerous skeletal muscle, the margin between dead and living muscle substance is formed in the last resort by the natural surfaces, or ends, of the cells not directly injured. If, notwithstanding these data, the standpoint of the pre-existence theory is adopted, there is nothing for it but to assume that each single cell of cardiac muscle is furnished at its ends with a parelectronic layer, just as in polymerous muscle a parelectronic layer must be assumed on either side of the tendinous intersection. But such a conclusion will hardly be subscribed to, unless inevitable. It follows therefore from the reaction of polymerous and cardiac muscle, that both the constituents of the former, and the cell elements of the latter, give no external electromotive response in the uninjured state.

Analogous experiments, undertaken by Engelmann on the organs composed of smooth muscle cells, yielded the same results. Here too, as in the heart, the E.M.F. sinks very rapidly between artificial transverse and natural longitudinal section, rising again when the section is refreshed, a reaction which may also be

witnessed in the adductor muscle of Anodonta. Each muscle-cell must therefore be regarded as free from current in the uninjured state. If the longitudinal current disappears entirely on injuring a polymorous muscle when the progress of rigor is arrested at the nearest tendinous intersection, the question arises whether there is no means of limiting the invading process of mortification from the artificial cross-section in a *monomorous* muscle, and thus abolishing the muscle current. The excised muscle cannot possibly be saved, but it is conceivable that if circulation were maintained, a muscle cut transversely might heal up again. Engelmann (*l.c.*) found in fact that ordinary skeletal muscle (frog's sartorius) did become gradually currentless again after subcutaneous incisions; if the artificial section loses its negative potential under the influence of normal conditions of nutrition, the natural ends of the fibres, during life, could certainly not be the seat of electromotive action.

All these facts concur to show that striated muscles are free from current when perfectly uninjured, and that the "current of rest in muscle" implies the existence of artificial cross-sections, mechanical, thermic, or chemical.

Passing to the different attempts at explanation of electromotive action in the injured "resting" muscle, it must in the first place be remarked that one of the two theories which till recently stood in sharp contrast must now be regarded as disproved, at least in the form in which it was originally propounded by du Bois-Reymond. Since Hermann's epoch-making work, the view has more and more gained ground, that in the complicated processes within the living substance, chemical action deserves at least as much attention as the physical symptoms, and that from any one given phenomenon it is not permissible to draw a parallel between tissue (*e.g.* living muscle or nerve) and a purely physical schema, and to treat it on this assumption. Yet on account of its historical interest, as well as in regard to future discussion, we must give a brief account of du Bois-Reymond's "molecular theory"; the more so because an attempt has recently been made to revive it, although in a different form (Bernstein). Moreover, it gives an opportunity of discussing some facts that are important to the sequel, with regard to the distribution of current in animal conductors.

If a body, such as the transversely bisected muscle, is the

seat of electromotive energy, the first essential is to ascertain its distribution of potential. How this can be effected with the help of a homogeneous, leading-off circuit, *i.e.* one which in itself, and by its application to the moist conductor, develops no differences of potential on contact with the surface of the electromotive conductor, has already been stated. It remains to show how far conclusions may be drawn from the distribution of surface potential as to the internal electrical conditions. Starting with the consideration of a regular column of fluid, in the centre of which, at any point of its axis, an electromotive force is in action, the lines of current in the plane of any longitudinal section may be represented by the accompanying diagram (Fig. 108).

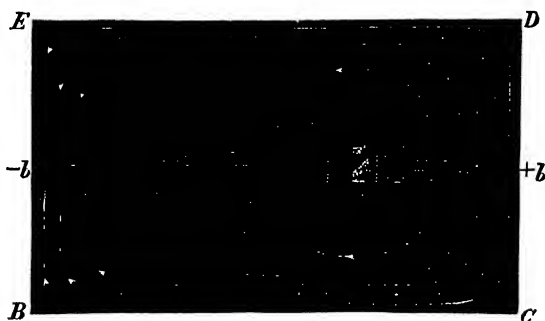


FIG. 108.—Diagram of current distribution in a column of fluid. (Rosenthal.)

If, *e.g.*, (*A*) represents a small body composed of two different metals in contact, the entire column will be traversed by lines of current in the direction of the outgoing arrows, which collectively form a series of planes (planes of current) lying one within the other. Corresponding with the “fall of potential” there will be, at each point of the path of current, a positive, or negative, potential, and it is easy to conceive a second system of lines or planes if each equi-potential point on the different lines or curves of current (planes of current) is joined together, as indicated by the dotted lines. These last curves, in which the intensity of current diminishes in proportion with increasing resistance—as they approach the surface of the column—are known as curves of potential, or *isoelectric curves*, which again form collectively a system of curved planes (planes of potential, *isoelectric planes*), cutting the planes of current at right angles.

Here, as in the regular muscle cylinder, the lines of intersection of the isoelectric planes with the surface of the column, form circles parallel with the periphery of the end-surfaces, the curves of current of meridional lines. Yet a perfectly definite seat of electromotive force cannot be forthwith determined, for an analogous distribution of surface potential may occur in many other cases, where it is at least doubtful whether electromotive forces are at work within the body at only one, or at several, or many places. As a matter of fact, each new seat of electromotive action implies a different system of lines of current and potential, *i.e.* a different distribution of surface-potential; but, as Helmholtz pointed out, seeing that in a complex of electromotive forces the potential of each point on the surface of the

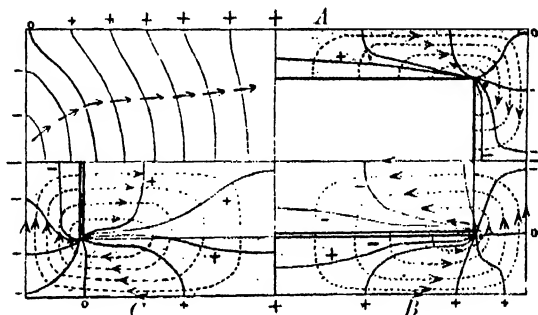


FIG. 109.—Schema of hypothetical distribution of electromotive planes in a muscle-fibre
Axial longitudinal section. (Hermann.)

body corresponds with the sum of the potentials brought into play at this particular point by each electromotive force respectively, we may conceive many combinations in which the same distribution of surface-potential would always present itself. Turning now to the case in which a cylindrical body exhibits a similar electromotive action to that which occurs at both ends of a muscle with parallel fibres, provided at either end with an artificial transverse section, we find (amongst others) that a solid copper cylinder with a zinc sheath corresponds with the required conditions when immersed in any conducting fluid, *e.g.* dilute H_2SO_4 . This, according to schema *A* (Fig. 109), is traversed by innumerable lines of current, which pass as a whole from the electrically positive zinc sheath to the electrically negative end-surfaces of the copper, exhibiting a distribution of surface-

potential analogous with that of the muscle prism. But the same result would ensue with two other presumptive dispositions of the electromotive planes. A hollow cylinder, *e.g.*, the surface of which is coated with zinc, may be filled with acid water, the entire apparatus being immersed in the same: schema *B* (*i.e.*) will then correspond with the distribution of potential. Lastly, if a hollow zinc cylinder with copper end-surfaces is examined under the same conditions, schema *C* will become effective (Fig. 109).

Which of these three schemata is actually realised in the muscle cannot *prima facie* be determined by experiment. In regard to the first, it must be further observed that (in the sense of the preceding observations) the one solid cylinder may be replaced by any number of little cylindrical or rounded bodies ("peripolar molecules"), each provided with positive longitudinal, and negative transverse, sections, provided they are regularly

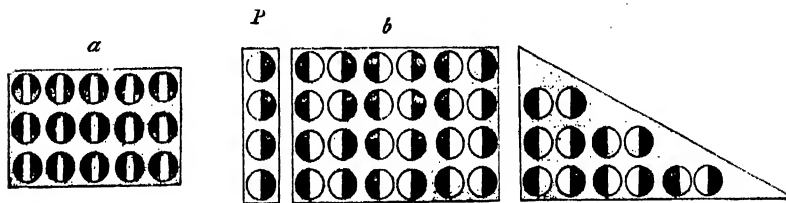


FIG. 110.—Schemata of peripolar (*a*) and dipolar (*b*) molecules. (Hermann's *Handb.* i. 1.)
Paraelectronic molecules at natural section.

arranged somewhat after the accompanying diagram (Fig. 110, *a*). With reference to the real anatomical relations of the muscle, the first case, in the modified form last stated, coincides with the molecular theory of du Bois-Reymond, the second with a hypothesis of Grünhagen, which postulates an electromotive opposition between muscle-fibrils and surrounding nutritive fluids, while, finally, the third is fundamental to Hermann's alteration theory, which presumes that electromotive action is set up at the artificial transverse section.

If any two points of different potential upon the neutral sheath are joined by a deriving circuit, a branch of the current will flow into this circuit, corresponding with a *fraction* of the internal E.M.F., since these currents, particularly in the immediate vicinity of the electromotive planes, undergo a large amount of short circuiting. Therefore, as already urged by Hermann, it is important in many cases to take into considera-

tion that the *internal current* can by no means be neutralised by compensation of the led-off portion of the current. "A muscle with a deriving circuit, of which the current is compensated, behaves as though the circuit were non-existent, and the currents completed themselves in the substance of the muscle." Du Bois-Reymond's comprehensive physical theory of the current in muscle (and nerve) starts from the fact that every particle of muscle that it is possible to examine, exhibits the same normal differences in potential between longitudinal and transverse section. Thus nothing prevents us from picturing the whole muscle and each single fibre as consisting of many little particles or molecules, every one of which has the same electromotive action as the entire muscle cylinder. These may either be conceived as spheres with two negative polar zones and a positive equator (peripolar molecules), or, as du Bois-Reymond assumed later in view of certain facts to be discussed below, as—in each peripolar electromotive molecule—consisting of two dipolar portions, of which the positive halves are convergent (Fig. 110, *b*). Accordingly, each artificial cross-section would fall between two positive, never between two negative, planes. For the rest it is quite immaterial what aspect we give to the individual molecules, they may as well be imagined discs as spheres. The regular arrangement of them, according to the accompanying diagram (Fig. 110), is the sole essential. If now the whole cylindrical, or prismatic, aggregate of these same electromotive molecules is conceived as surrounded by a thin sheath of some indifferent conductor (perimysium, sarcolemma, dead layer at the cross-section), the distribution of potential at the surface will, as has been shown, correspond throughout with the real experimental conditions. With the aid of this hypothesis it is possible indeed to give a simple explanation of all phenomena of the "current of rest" in the muscle, more particularly the fact of the homodromous activity of each least particle of muscle, as well as the so-called "Neigungstrom" in oblique sections. The interpretation of parelectronomy, however, presents difficulties which, on the pre-existence theory, can only be explained by the further assumption as above, that a specific compensating layer is situated at the natural transverse section, figured by du Bois-Reymond as consisting of "parelectronic molecules," whose positive surfaces turn

towards the tendon, and may be derived from the inner half of the externally situated dipolar molecules. When the parelectronic layer consists of a whole series of dipolar molecules arranged in columns a "parelectronic tract" results. Bernstein (13) has recently modified du Bois' molecular theory in certain essential particulars, endeavouring to give it a new basis as the "*electro-chemical molecular theory*." According to him the living fibres must be presumed "to consist of a longitudinal series of molecules, aggregated into fibrils of a finite diameter, lying in a congruent fluid, from which they derive their nutrition (paraplusma)." They are linked together by forces, "which may be regarded as identical with, or akin to, chemical affinity," and consist of a nucleus of complex chemical constitution, identical with Pfliiger's living molecule of albumen. The long sides of

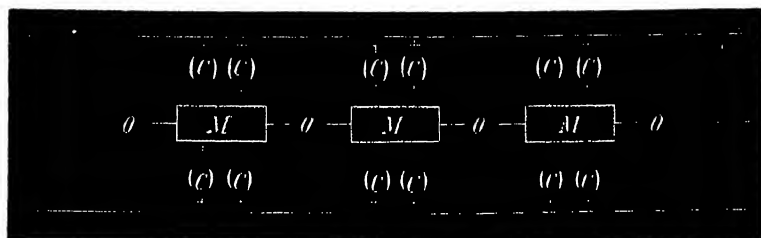


FIG. 111.

the molecular nucleus (M), conceived as a prism (as in Fig. 111), the end-surfaces being linked together loosely by atoms of oxygen, are described by Bernstein as "laden with oxydisable non-nitrogenous groups of atoms, comparable with fine platinum wires, dipping into an atmosphere of hydrogen." "The rows of molecules, bathed in nutritive fluid, constantly draw out of it the charges essential to metabolism." "If these are regarded as electro-positive in relation with the molecular nucleus, the oxygen atoms on the other hand as electro-negative charges of the same, the current of rest in the muscle (and nerve) results when the longitudinal surface is connected with an artificial cross-section. It may also be assumed that on making an artificial section the tearing apart of the chain of molecules sets free assimilated oxygen, which would be negative in potential to the molecular nucleus." The parelectronic condition of the ends of tendon would be explicable on this theory, if it is assumed "that each such

series of molecules constantly passes over into the adjacent series by a loop-like circuit, and thus presents no free cross-section." If a single such "molecule," or better, aggregate of molecules, lay singly embedded in a conducting fluid, it would evidently react in every particular like a peripolar molecule of du Bois; collectively, however, these cannot, like the latter, be conceived as surrounded by molecular currents, since the potential on all sides seems to be neutralised. The same objections as obtain against the original molecular theory also to a great extent apply to its "electro-chemical" translation, while the excessively detailed presumptions of the latter *re* chemical structure of living substance must *a priori* give rise to much reflection.

According to Grünhagen's theory, we must assume an electromotive opposition between each primitive fibril and the surrounding nutritive fluid (sarcoplasma), whereby the latter represents the positive, the fibrils the negative, link of the chain. The absence of current in uninjured muscles would, on this theory, be very simply explained by the immersion of the negative electrical fibrils in the positive nutritive fluid. Grünhagen's views of the cause of electromotive action in animal tissues originated in experiments with porous cylinders. Yet, as Hermann points out, it is difficult to see how these experiments apply to the given relations in muscle. Grünhagen found, namely, that cylindrical, porous bodies, during the moistening of their cross-sections (end-surfaces), exhibited difference of electrical potential towards points in the middle of their longitudinal surface, and also between asymmetrical points of the two surfaces in themselves—in the same direction as the muscle cylinder. These differences of potential disappear when the porous cylinder is saturated with fluid, and is therefore to be viewed as an effect of the *passage* of fluids through the porous substance. Grünhagen imagines the relation between fibrils and surrounding nutritive fluids to be similar.

The third theory relative to the seat of electromotive action is the *alteration-theory* of L. Hermann, which is in perfect agreement with all the facts known to us. This theory refers all electromotive activities of living tissue to chemical changes of the substance without regard to its molecular structure. With reference to the "resting" muscle current, the theory proceeds from the postulate, "that dying substance is negative to living substance."

The seat of electromotive action must accordingly be referred to the margin between dying and living substance ("demarcation surface"). Hermann therefore designates the "current of rest" in the muscle, the "demarcation current." Hering (14) has recently expounded Hermann's principle of interpretation on very general considerations. The proposition that uninjured resting muscle or nerve has no current implies to him "that such a tissue does not develop a current that can be led off externally, so long as its metabolism, *i.e.* the internal chemical action in all its parts, is equal. Every disturbance of equilibrium sets up currents that can be led off." Hering also emphasises the fact already brought forward by Hermann, that alteration of chemical action in any part of the living continuum may appear not merely "in that the part concerned becomes negative to the unaltered parts, but also that it may become positive to the same." If then the part that differs chemically from the remaining substance is termed (relatively) *altered*, we must distinguish between "*a (relatively) positive and a (relatively) negative alteration*," to which must be added that "the alteration is characterised not by altered chemical composition, but by altered chemical action, which may of course give rise to altered composition." As has been shown in another section (*e.g.* fatigue in muscle), Hering distinguishes in every living substance between the ascending alteration, the descending alteration, and the state of equilibrium.

"Both 'up' and 'down' changes may occur with very different rapidity, according as the strength of assimilation exceeds that of dissimilation, or *vice versa*, to a greater or less extent. If all parts of a living continuum are equipotential, or if they alter with the same rapidity in an ascending or descending direction, no current that can be led off will be produced. Each variation in rapidity, or direction of alteration, will, however, produce a current that can be led off. Accordingly, we may conceive every variation in rapidity of the positive or negative alteration, as arranged in a series, so that the quickest ascending change formed the upper, so to say, positive—the quickest descending change, the lower, so to say, negative end of the series. If two portions of a living continuum which give different chemical reactions are connected by an external conductor, they will *ceteris paribus* yield a stronger current in proportion with the distance between the two leading-

off points in the series mentioned, and the positive current always flows through the external circuit from the point nearest the positive end of the series to that which is nearest the negative end. *This is the law of all vital currents in nerve and muscle.*

"A sartorius exposed with all possible precaution, *e.g.* one that is no longer normally nourished, undergoes a slow and steady descending alteration, because dissimulation preponderates over assimilation; it is slowly dying.

"If this descending change proceeds in every part at exactly the same rapidity, the most sensitive galvanometer will fail to detect any current. This ideal case is never of course fully realised. But with even a moderately sensitive galvanometer, no current will be detected in such a muscle, as was shown by du Bois-Reymond, as well as later observers. On making a cross-section in the muscle, a more rapid descending change at once appears in the muscle-substance; the part immediately adjacent to the section mortifies. This dead part is no longer included in the living continuum, and must be regarded as an inessential appendage. The more rapid 'down' change and mortification, however, proceed *pari passu* along the fibre, as may be verified under the microscope, and after making a transverse section, there is always a more rapid descending alteration than in the other fibres. *The cross-section is therefore negative to the longitudinal surface of the muscle.*"

But it is not merely by theoretical considerations, in addition to its extreme simplicity, that the Hermann-Hering theory is distinguished from all others. There are also direct experimental facts in its favour, which may be taken as proven. Among these, apart from all previous experiments on the absence of current in uninjured muscles, is that by which Hermann tries to determine the question whether the development of the demarcation current, on making an artificial cross-section, takes a perceptible time, or whether the full value of the P.D. between longitudinal and transverse section is reached immediately after injury, as must necessarily be the case under the presumption of pre-existence of electromotive forces. For this purpose Hermann constructed a "fall" rheotome, in which the expansion of the tendo achilles was torn away from the gastrocnemius by a heavy falling body, the galvanometer circuit being simul-

taneously closed for a short period. If this closure is effected once at the moment of injury, and again after making the section, the deflection in the latter case will be greater than in the former, from which a "period of development" of the muscle current may be concluded. Hermann carried out similar experiments with the same results on muscles with parallel fibres (15).

The correctness of these theoretical presumptions as to the causes of animal (and vegetable) electrical currents, and the justification for rejecting every molecular hypothesis whatsoever, are attested by the author's demonstration of the *direct dependence of the muscle current on local chemical changes in its substance*. If it is correct that in muscles and nerves, as in other animal and vegetable tissues also, the electrical differences of potential which may be demonstrated under certain conditions may always be traced in the last resort to the different chemical reactions between adjacent parts of the living substance, it must *a priori* be granted as possible that the resulting electromotive action can be neutralised again, in so far as there has not been such total destruction as to prevent restoration of the normal activity of the chemically altered substance. It is known that even excised muscle possesses to a certain extent the capacity of readjusting chemical changes in its substance, produced by certain excitants (stimulants), e.g. "recovery" in "fatigued" muscle. We have already drawn attention to the interest of the fact that, independent of previous excitation, a muscle may be thrown into a state resembling fatigue by submitting it to the action of certain chemical substances ("fatigue-substances"), after which, by washing these out with an indifferent fluid, it can be restored to its normal excitability (Ranke). It then becomes essential to investigate how far electromotive action may result from the contiguity of fibres which are chemically altered, but still capable of recovery, and fibres that are in normal chemical activity. Ranke's investigations of "chemical fatigue of muscle" by salts of potash, or lactic acid, the striking effect of which upon the phenomena of polar excitation by current has already been discussed, appear to promise the best results. It is found that after brief immersion of one end of a sartorius that is free from current, in a dilute extract of muscle tissue, or highly dilute solutions of potassium salts (KNO_3 , KH_2PO_4 , KCl), it becomes strongly negative towards every other point of

the muscle. The size of the deflection was in many cases a little smaller than when a sartorius provided with an artificial cross-section is connected in circuit from cut surface to corresponding point of the upper surface. Here diminished excitability goes hand in hand with negativity of muscle-substance, and just as this may be simply neutralised by washing out with physiological NaCl solution, so too in regard to current. A few minutes suffice to reduce the P.D. to a mere trace, which, with longer washing, is also abolished, so that the muscle is once more—as at the beginning of the experiment—free from current and of normal excitability. The same result is obtained from the currentless (parelectronic) gastrocnemius by painting the expansion of the tendo achilles with fluid, and the ascending current obtained in consequence is well developed and of the same order as the normal demarcation current (16). This very fact, however, makes it the more remarkable that the “potassium current” should be so easily neutralised by washing out with an indifferent fluid, as is once more exhibited in a striking manner on the gastrocnemius; it suffices, after the muscle-substance at the tendo achilles has become strongly negative from painting with dilute solution of potass-salt, to wash it for a few moments with 3–4 % NaCl solution, in order—as with the galvanometer—to replace the original, currentless condition. This shows that the prejudicial effect of the solution can only have extended to the extreme ends of the obliquely inserted fibres. From these experiments the current-developing properties of every artificial cross-section of a muscle are also easily interpreted, since acid potassium phosphate is always formed when the muscle-substance becomes rigored.

In opposition to the “potassium currents,” those differences of potential which appear on treating currentless muscle in the same way with very dilute acid solutions (*e.g.* lactic acid) seem to depend on much deeper chemical changes in the muscle-substance, since no amount of washing will neutralise them, although they are weaker than those produced by salts of potash.

Du Bois-Reymond laid down the principle that no more delicate test of the chemical sensibility of the muscle-substance to any fluid can be devised than to moisten the natural cross-section of a parelectronic muscle with the solution, and to observe the changes thus produced in the electrical condition of

the section. From this point of view, the potassium salts in general must be regarded as distinct muscle poisons, while the corresponding sodium combinations at the same molecular weight are almost innocuous, and even possess in many cases a distinct power of regenerating excitability (Na_2CO_3). In consideration of this last fact a fluid cannot therefore be termed indifferent for the muscle, where no perceptible current is developed from its local application. Even the physiological NaCl solution (0.5–0.7 %) which, if applied for hours to the natural cross-section of an uninjured, currentless muscle, causes no trace of a demarcation current, produces, according to F. S. Locke (17), a visible increase of excitability, as has long been known with regard to stronger solutions. Certainly, however, the current-developing properties of a solution must be taken as the measure of its *injuriousness* to the muscle, and though Nasse takes a 0.7 % solution of KCl or KNO_3 as equal to a 0.2–1.5 % solution of NaCl, his conclusion is not borne out by galvanometer experiments. If the lower end of a curarised sartorius dips into even a 2 % solution of NaCl, no perceptible demarcation current will have appeared after 10 to 20 minutes, or there may even be a faint deflection in the opposite direction, in the sense of a descending current in the muscle. Engelmann, too, found in his investigations into the electromotive properties of the uninjured surface of the frog's heart, that solutions of NaCl, if stronger than 0.6 %, made the points in contact with them *positive* in regard to other points of the surface of the heart. Still less deleterious than NaCl is the action of other neutral sodium salts upon the substance of the muscle, *e.g.* Na_2SO_4 and NaNO_3 , which, even in strong solutions (4–12 %), develop only a small amount of current, as compared with the local effects of equivalent solutions of NaCl or the corresponding salts of K upon the sartorius. Even alkaline sodium carbonate, which augments the excitability of striated muscle in a remarkable degree, either produces no current in dilute solutions, or a weak inverted current only, in the sense of positivity of the immersed end of the muscle (18).

The opinion generally prevails that distilled water is rapidly and energetically inimical to muscle-substance, *e.g.* Kühne concludes from the fact that a frog's sartorius dipping into distilled water loses its excitability more quickly than a muscle dipping

for the same time into nitric acid (HNO_3), that the water has a quicker destructive action than the dilute acid, and du Bois-Reymond states that a gastrocnemius dipping into distilled water (15°C.) was death-rigored and acid within an hour. Consequently one might have expected, if the development of current in a "parelectronic" muscle depended only upon the destruction of a particular layer at the natural cross-section, that on moistening it with distilled water, a powerful, normal current would in a short time be apparent, since it is proved by experience that the current-developing property of a fluid is quite independent of its conductivity. This is partly contradicted already in the experiments of du Bois-Reymond, since the development of current in parelectronic muscles, on dipping them into distilled water, proceeds weakly and sluggishly. The sartorius reacts even better. If the knee-end dips into water, an increase of volume is perceived in it shortly after, and it will then regularly be found weakly *positive* to points of the normal surface. After longer duration of the action of water (20-40 minutes) the muscle section is much swelled, and double its former breadth; it looks very dark, and exhibits all the external signs of rigor. At the same time the partially rigored muscle shows as little electromotive action as before, or there may still later be weak signs of a normal demarcation current. Even after hours of the action of distilled water, the demonstrable P.D. of the two sections of the muscle is, in spite of the marked differences in their physical properties, relatively insignificant, and not to be compared with those which underlie the normal demarcation current between longitudinal surface and artificial cross-section (18).

When we remember that all known methods which throw the contractile substance of the muscle into rigor (heating to 40°C. , treatment with chloroform, acids, etc.), produce powerful demarcation currents on local application, the absence of electromotive action in the partially water-rigored sartorius is very significant, since it would appear not to harmonise with a chemical theory of the muscle current. In opposition to this it must be remembered that the condition of "water-rigor" cannot be immediately identified with the deep-seated chemical alteration of the muscle-substance, due to spontaneous or sustained rigor, or to heat-rigor. This, because on the one hand

the acidity, where it appears, by no means proceeds *pari passu* with the progressive development of "rigor," while on the other the possibility of recovery of excitability in water-rigored muscles by simple dehydration (2 % NaCl solution) is evidence that the coagulation effects are of another kind than the ordinary forms of rigor. The difference between water-rigor and other forms of rigor is best shown by the fact that frog's muscle, in an advanced stage of water-rigor (an hour or more), exhibits electromotive action in the same sense and almost in the same degree as uninjured muscle. If the lower end of a vertically dependent sartorius dips for 30 minutes into distilled water, the muscle will usually, as stated above, show no current, on leading off from the geometrical equator and water-rigored section, or it exhibits a weak inverted current. But if part of the moistened muscle section is warmed in water at 40° C., it exhibits, on leading off, the same electromotive action as before; the same is the case after crushing or cutting the water-rigored end. There can therefore be no doubt that there is chemically a fundamental difference between the effect of the *rigor-like* condition produced by distilled water, and the true *rigor-mortis* of a muscle, the complete development of which seems to preclude the possibility of electromotive activity. As therefore electromotive function must certainly be regarded as a property of the *living* muscle, it is the more remarkable that it should in no way be bound up with the continuance of *all* vital properties. It can be shown, *i.e.* that the demarcation current persists in its normal direction and proportions where the muscle has been rendered inexcitable by chloroform, ether, or amyl. Ranke, who was the first to make these observations, always exposed the whole uninjured frog to the vapour of the anæsthetic, and examined various stages of the narcosis. A quicker method is to place the free sartorius, with an artificial cross-section, along with the leading-off electrodes, and a watch-glass of ether, under a bell-jar that is not too small. It may easily be seen that the P.D. between longitudinal and artificial transverse section does not diminish to any perceptible degree, and sometimes even appears to be augmented, when all visible manifestations of excitation have failed in the muscle (19).

While contractility and conductivity for the most part seem to be abolished in 10–15 minutes, but little diminution

of the demarcation current can be observed, even after hours of exposure to ether vapour, which is the more remarkable when it is considered that all the influences which depress excitability have also a general diminutional effect upon the muscle current. If then, during ether narcosis, a muscle—of which the excitability seems to be entirely abolished—has no less pronounced an electromotive reaction than under normal conditions, the presumption is that the changes in chemical activity of the muscle-substance, which must always be reckoned with in the proximity of a cut surface, persist during the ether narcosis to the same degree as under normal conditions. Another fact of the same significance is that local treatment with salts of K in correspondingly dilute solutions also renders the ether muscle negative at the point of contact. Further, remembering the persistence of the normal physical properties of the narcotised muscle at a time when, even with the strongest excitation, there is no trace of visible change of form, it does not appear so surprising that a muscle, even in the deepest narcosis, should still be capable of electromotive response, although some of its normal vital properties may be fundamentally affected or entirely abolished. For if it is admitted that the “current of rest” owes its origin to a partial “alteration” in the substance, it would follow that it may be expected in all those cases in which the preparations concerned have not been fundamentally disturbed in their normal, chemical composition; and this both in respect of ether, and of turgescence of the muscle from water. Later on we shall have to discuss other facts which indicate that conductivity and contractility of the muscle are primarily abolished by narcosis, while local excitability persists in the sense that certain chemical changes still occur under the influence of chemical stimuli, which, *inter alia*, go hand in hand with negativity of the points in question.

II.—THE CURRENT OF ACTION

A complete account of the earlier theories of electrical activity in muscular contraction would here be out of place since, like the history of the “current of rest” in muscle, the subject has been thoroughly reviewed by du Bois-Reymond, in Part II. of the “*Untersuchungen*.” It is enough to recall

the fact that an electrical theory of muscular contraction was founded by Prévost upon certain observations of Ampère, as early as 1837, and this is of interest, inasmuch as it shows to what extent physiological conceptions may be influenced by current physical theories. Prévost convinced himself by microscopic investigation that the cross-striation of the fibres of skeletal muscle was simply the optical expression of looped nerve-endings lying parallel with one another, which pull in opposite ways at the moment when an electrical current traverses the entire system of loops in the same direction. In order to demonstrate this current, Prévost introduced a "very fine non-magnetic needle into the frog's leg in the direction of the fibres; the point projected, and was covered with iron-filings"; at the moment at which a vigorous contraction was produced by injury to the spinal cord, the iron-filings were said to arrange themselves round the point of the needle, as if they had been magnetised. A similar theory was advanced by Wharton Jones in 1844 (du Bois, *l.c.* p. 10). "According to his view, which follows on with Bowman's observations (composition of muscle-fibres out of 'discs'), the muscle-fibres consist of discs arranged in columns, or rouleaux, connected by a flexible and elastic substance, which enable them to approximate, or recede from one another. The discs, according to Wharton Jones, are converted by the influence of the nerve into electro-magnets, and their antagonistic traction produces the shortening of the muscle. The electro-magnets ("appareils nervo-magnétiques") are not indeed surrounded on all sides by nerves, as an iron magnet would be with copper wire; this only proves, however, that nature adapts itself to simpler arrangements. The first real advance in this department is once more owing to that indefatigable worker who discovered the muscle current almost simultaneously with du Bois-Reymond. C. Matteucci, after taking infinite pains, from 1838, to demonstrate electrical action during muscular activity, and repeating *inter alia* the experiments of Prévost in different forms, succeeded at last in discovering a fact which gave the required determination. On February 28, 1842, Matteucci communicated to the Paris Academy the account of an experiment which must be reckoned among the most elegant and interesting in experimental physiology. This was proof of what du Bois-Reymond afterwards

termed "secondary contraction," in which the leg of a frog twitches vigorously when its nerve is laid upon the muscle of an excited second leg. In the same year Matteucci received the prize for experimental physiology from a Committee of the Academy, which included the older Bequerel, and the renowned physicist concluded from the experiment, which was recognised as valid on all sides, "that an electrical discharge must take place in the muscle at the moment of contraction, and finds its way in part through the nerves of the second frog." Matteucci had previously observed that the secondary contraction was not obstructed by moist filter-paper, while on the other hand it was stopped by gold plates or non-conductors, laid between the nerve of the secondary preparation and the muscle of the primary. These results are in complete agreement with the theory as stated. Matteucci, on his side, was eager to find new proofs of the presumptive development of electricity in contraction—compared directly by Bequerel with the stroke of the torpedo. As early as 1845, a new publication appeared in English on the "induced contraction," as it was now termed by Matteucci. He had found its appearance to be independent of the position of the secondary nerve on the muscle of the primary preparation; it may be laid parallel with the fibres, or across them, or in any direction; the secondary contraction invariably follows. Matteucci cut a disc of muscle out of the leg with a razor; the secondary contraction never failed, provided the testing nerve was in contact with the cut surface. He further obtained twitches of the third and fourth order by placing the nerve of a second test-preparation upon the gastrocnemius of the first, the nerve of a third preparation on the muscle of the second, and then exciting the primary nerve. With regard to the presumably electrical nature of the secondary twitch, Matteucci moistened the surface of the first muscle with different conducting and non-conducting fluids, *e.g.* serum, blood, oil, and dilute alcohol, varnish, oil of turpentine, etc., in which the nerve of the second preparation was bedded. In none of these did Matteucci find the twitch abolished, although this happened with the thinnest plates of a firm body, *e.g.* glass, talc, etc. The skin of the frog, like filter-paper, was favourable to secondary contraction. These last observations misled Matteucci in regard to the prevailing theory of the electrical origin of secondary

contraction, and he believed himself to have discovered a special force, manifesting itself by action at a distance, which proceeds from the muscle at the moment of contraction; this led him to give the name of "induced twitch" to the phenomenon he had discovered.

Up to this point Matteucci had no knowledge of a discovery made by du Bois-Reymond in 1842, in following up an older investigation of the Italian experimenter. As far back as 1838, Matteucci had discovered that the ascending current in the frog ("courant propre")—as demonstrated by Nobili in 1827 with Schweigger's multiplier on galvanic preparations, and referred by du Bois to the current of the single muscle—disappeared altogether, or was much weakened during tetanus (later, he believed himself convinced of the contrary). Du Bois-Reymond, who had meantime formulated the "law of the muscle current," went on to ask, How the muscle current behaved during persistent excitation? The first communication of the weighty results of this inquiry appeared in 1842, in a "preliminary sketch." In this it was shown that the longitudinal transverse current of the gastrocnemius did not disappear during contraction, when the nerve was tetanised, but that it did diminish perceptibly in intensity.

The capital experiment of this investigation was originally arranged as follows (Fig. 112). The gastrocnemius lies with its longitudinal and artificial (or corroded natural) transverse sections upon the pads of the leading-in dishes; the central end of the nerve is stretched over platinum electrodes, connected with the tetanising apparatus. The experiment invariably results in an unmistakable diminution of the muscle current during tetanus, a *negative variation*, as seen in the backward swing of the needle of the multiplier, or circular magnet of the galvanometer. All possible objections and sources of fallacy were investigated by du Bois-Reymond with his usual thoroughness, and he succeeded in establishing beyond doubt that a diminution of E.M.F. does actually accompany the state of excitation. In later experiments du Bois investigated the negative variation, with similar results, on the regular parallel-fibred muscles of the thigh, instead of the complicated gastrocnemius, change of form in the muscle being avoided by tension between two fixed points. The method of compensating the "current

of rest" as introduced by du Bois, has the distinct recommendation that it shows the negative variation to be a deflection contrary in direction to the original effect, its distribution in time, which is accelerated at first with an aperiodic magnet, becoming gradually slower. On prolonging the excitation there is a slow return to the position of rest, which is sometimes reached during the closure of the circuit, in other cases only after it has been opened again; but the return is seldom perfect. There is usually a permanent

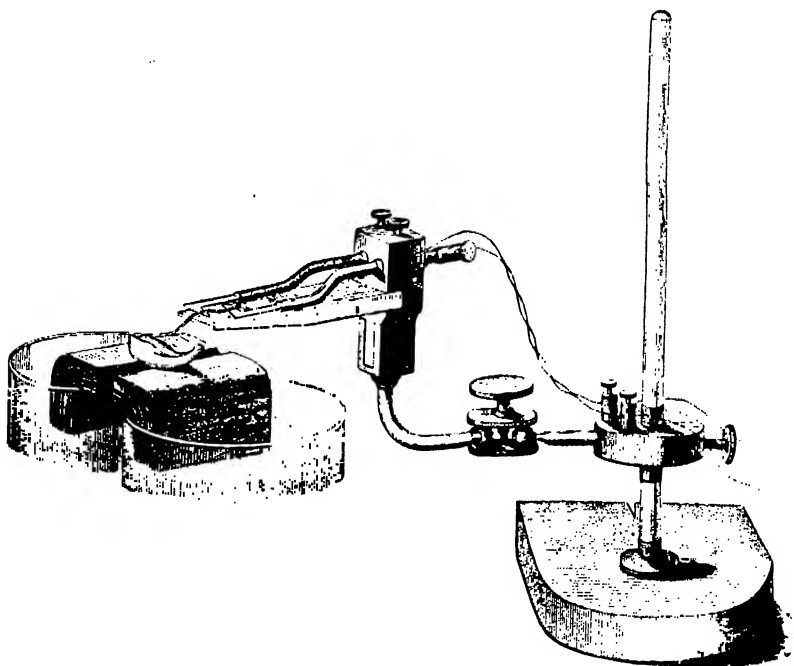


FIG. 112.

diminution of the muscle current (negative after-effect), the degree of which depends on the strength of the previous excitation.

The immediate inference as to the meaning of the backward swing of the magnet during tetanus would be, that there was a *persistent* diminution of the longitudinal current, continuous throughout the period of excitation. In view, therefore, of the known properties of the physiological rheoscope, which reacts mainly at the rise or disappearance, or sudden variations in density of a current, it might be expected that the leg serving

to test the current would contract in consequence of the rapid decrease in current at the beginning of tetanus, if the nerve bridged over the longitudinal and transverse sections of the excited muscle. On the other hand, we should hardly look for this result at the end of tetanus, since the muscle only returns gradually to its original condition. This experiment, as tried by du Bois-Reymond, yielded a very striking result, not at all in correspondence with what was anticipated. The test-limb, *i.e.*, not merely twitched at the beginning of tetanus, but actually fell into secondary tetanus during the whole of the primary excitation. If this is imperfect, so that each single twitch remains recognisable, and the muscle is then connected on the one hand with the galvanometer, and on the other with the physiological rheoscope, the latter responds by a secondary twitch to every primary contraction, while the magnet, in consequence of its sluggishness, swings back simply in the direction of the negative variation. We may, therefore, and indeed must suppose that even with the most complete fusion of the visible contractions of the primary muscle, into sustained tetanus, each impact of stimulation calls out an excessively short negative variation, distinct in time from that which succeeds it, so that the muscle current fluctuates, as it were, up and down in the rhythm of the tetanising stimulus, by which we see that notwithstanding the apparently steady contraction of the muscle in tetanus, it really originates in *discontinuous* alterations of state, exhibited more especially in its galvanometric response as above. The extraordinary superiority of the physiological rheoscope to all other known physical apparatus for testing current is obvious, and it is only quite recently that a method has been discovered which (with regard to the possibility of demonstrating variations in current lasting for a short period only, and following in rapid succession) may be compared with the faithful response of the physiological rheoscope to the electrical fluctuations. The accompanying diagram (Fig. 113) gives a clear picture of the behaviour of the muscle current in tetanus as attested from observations on secondary tetanus.

“ If the abscissa (σ , t) represents the time, on which the amplitude of the current is drawn at each second as ordinate, (σ , σ) further represents the constant magnitude of the muscle current in the state of rest; for, in order merely to produce a diminutional effect in the multiplier, it is indifferent whether (σ , σ) becomes

persistently smaller, as in (b, p, g) , or whether this occurs spasmodically, so that the current may sink much deeper, and even below the axis of the abscissa (which indicates reversed direction of current). The effect upon the galvanometer is the same in both cases. In the physiological rheoscope it is quite different. The form of the curve (b, p, g) would never produce tetanus in the test-limb; we are reduced to the assumption that it is the jagged curve, though with constant (unknown) depth of declinations, which really occurs in tetanus" (du Bois-Reymond). In order to deal fairly with the actual circumstances, it must also be noticed that each individual elementary curve of variation fails, in consequence of the after-effect, to reach the height of the original ordinate, so that the base-points of the single curves form a descending staircase, as in Fig. 113. Supported by these facts and hypotheses, du Bois-Reymond believed himself justified in propounding a general theory of Matteucci's secondary contraction, representing it simply, *i.e.* as *the physiological effect of the negative variation of the muscle current* present in every single twitch, and only marked by the sluggishness of



FIG. 113.—Negative variation in tetanus.
(Hermann.)

the magnet. (It is to be noted that the modern galvanometers with light, aperiodic magnets present no such difficulty, and the demonstration is as certain as in the physiological rheoscope). According to this view, du Bois held it to be a necessary condition for the appearance of the secondary twitch, that the nerve of the secondary preparation should occupy a definite position upon the primary muscle. According to his first results, the secondary contraction only appears regularly "when the nerve closes the circuit between the two dissimilar surfaces of the muscle (longitudinal and transverse section)." Matteucci had meantime found the appearance of the secondary contraction to be fairly independent of the position of the nerve upon the primary preparation, and had even placed it so that it formed a loop round the twitching muscle. It is, in fact, very

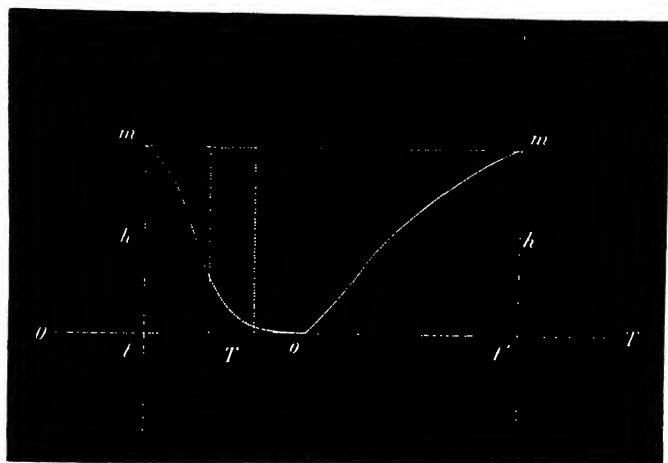
easy to prove that the secondary contraction is by no means *invariably* due to negative variation of a pre-existing current, as was admitted later by du Bois-Reymond himself, when he investigated the negative variation of "parelectronic" muscle.

Before pursuing this point any further we must, however, attack another question, which was left in abeyance in an earlier connection. It was stated that appearance of secondary tetanus might be taken as a proof that the muscle current undergoes no *continuous* diminution during contraction, but that during that time it is constantly varying backwards and forwards, although these movements are not followed by the magnet, on account of its sluggish reaction. The rheoscopic limb of the frog, however, leaves us in doubt as to how nearly the summits of the single curves of variation approximate to the zero line (indicated by dots in Fig. 113)—whether they do reach it, so that the current is *nil* at the moment of contraction—or finally exceed it, which corresponds with a reversal of current.

Du Bois-Reymond himself attempted to solve the first question (*Untersuchungen*, ii. p. 120), and with this object constructed apparatus "by which the muscle could be submitted to a rapid series of excitations through its nerve, moment by moment, in rapid succession. After each moment of excitation, the muscle current could be closed for a brief period, and this closure might follow at a given time between any two stimuli. If the muscle current therefore sinks between any two stimuli during tetanus in a normal curve, and then rises again, its deepest point will be reached so soon as the closure of the muscle current coincides in position with this point." The problem is still better expressed in the accompanying diagram (Fig. 114).

Let the abscissa (O, T) represent the time, on which are drawn the ordinates, *i.e.* height of the muscle current (h), so that the line (m, m), etc., corresponds with the line of the current during rest. In the equidistant moments of time (t, t^1, t^2, t^3), etc., there is always an excitation of the muscle, which results in a negative variation of the existing "current of rest," and its course, as will be shown, represents the curve (m, o, m), between each two stimuli. The true form of the latter is easily determined if the galvanometer circuit is closed between every two excitations, for a moment only (T), at periodically repeated and uniform intervals (t^1, t^2, t^3 , etc.) The same

segment (the hatched part of the curve, Fig. 114) is therefore always cut out of the superficies of a variation curve, and through its summation a deflection of definite proportions is produced. And, since the time of galvanometer closure can be prolonged as required over the entire interval between the two stimuli, the form and magnitude of the curve of variation corresponding to each single stimulus are easily determined. The credit of having constructed apparatus that satisfied these requirements belongs to Bernstein (20), whose "differential rheotome" has since found an extended application in experimental physiology. The instrument consists essentially of a wheel (*v*) (Fig. 115)



revolving easily round the central axis, worked as uniformly as possible (5–10 revolutions per second) by clockwork, or a small motor. At the periphery of the wheel there are three isolated metal-points (according to Hermann, brushes of copper-wire), one of which (*c*) forms the exciting contact, the other two (*c'*, *c''*) effect the closure of the galvanometer circuit. The former slides at each revolution over a thin extended wire, or pool of mercury, and thus closes the circuit (*R'*, *R''*) of the primary coil of an induction apparatus. The currents produced in rapid succession in the secondary coil (make and break shock) are led into the preparation, and may be regarded collectively as a momentary stimulus. Diametrically opposite to the exciting contacts, isolated from the

metal wheel, but in circuit with one another, are the two points (brushes) forming closure of the galvanometer, which at a certain point of the revolution pass through the mercury pools of two isolated steel cups (g^1, g^2), or over amalgamated copper contacts included in the galvanometer circuit (B_1, B_2). The pools (contacts) are movable, so that the duration of the simultaneous dip, *i.e.* duration of galvanometer closure (T), can be altered within a wide margin. Now, instead of extending this interval over the surface of the curve of variation as above, the distance of the time (T) from the moment of excitation (t, t^1), etc., is regulated in Bernstein's instrument by alteration of the slider

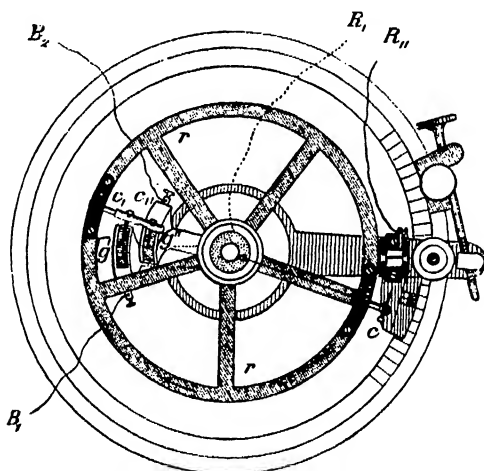


FIG. 115.—Bernstein's differential rheotome (seen from above).

which carries the exciting contact. The whole arrangement of the experiment resembles the diagram (Fig. 116). Owing to the complicated structure of the gastrocnemius, the sartorius is better adapted for the study of the negative variation, its demarcation current being compensated to start with. In consequence the galvanometer magnet remains at rest during rotation, and is only deflected when there is an alteration of the muscle current during the time (T). If the slider is then arranged, as in Fig. 116, so that the closure of the circuit of the primary coil occurs at the same moment at which the galvanometer circuit is broken by the two contacts, a complete revolution occurs before the closure of the muscle

circuit repeats itself, and if the process of negative closure has run out during this period, no deflection will be obtained. On actually working the experiment, however, we still find a negative deflection increasing slowly throughout the entire period of excitation, *i.e.* in the direction of the compensating current, due apparently to the diminutional after-effect of excitation upon the muscle current as described. Now, if the exciting slider is brought more forward, so that excitation occurs while the galvanometer contacts are still dipping into mercury, we find

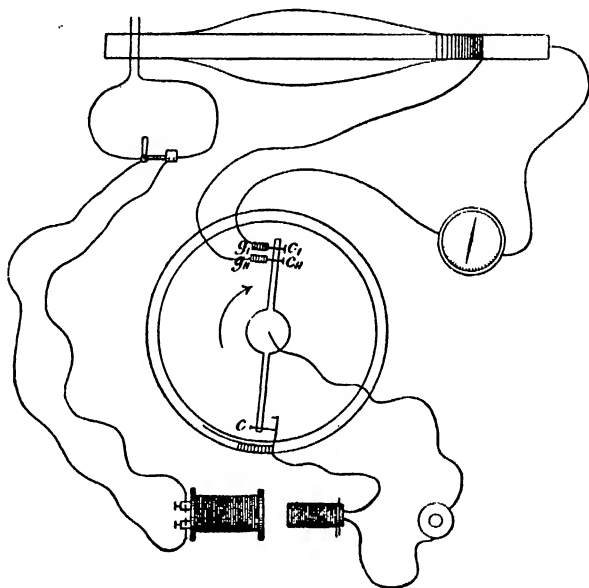


FIG. 116 — Schema of rheotome experiment. (Bernstein.)

at a particular point a *sudden increment* in the deflection, which increases rapidly in the negative direction on pushing on the slider, and finally reaches a maximum, after which it decreases again with further displacement of the slider, and at last remains persistently lower than it was at the beginning of the excitation. This shows that there is a measurable interval between the moment of excitation at one point of a muscle with parallel fibres (Bernstein always chooses the lower end of the sartorius as being free from nerves), and the beginning of the negative variation at the other, provided with an artificial cross-section;

also that the negative variation in the tract of muscle led off, itself has a certain duration. For on pushing the slider along, the deflections increase to a maximum, at which they persist for some time; but if it is pushed still further forward, no adjustment will produce a deflection of the magnet. The slider may be pushed over the whole graduated circle, without any repetition of the galvanometer deflection, until it has passed back beyond its first position, and reaches that in which the first negative deflection became apparent. The experiment therefore confirms the conclusions derived from the observation of secondary tetanus, to the effect that the negative variation of the muscle current on tetanising corresponds not to a *continuous* diminution of P.D. between longitudinal and cross-section, but to a discontinuous waxing and waning in the rhythm of the excitation. We see further that each single negative variation comes into existence more rapidly than it vanishes; graphically expressed, its curve rises steeply to a maximum, and then sinks slowly down again (cf. Fig. 114). If the rate of revolution of the rheotome wheel, and the distance expressed in degrees between the original position of the slider (when simultaneously excited and led off), and that at which the first deflection occurs, is known, it is easy to calculate the time (relatively to the length of muscle between the point of stimulation and the leading-off contact on the longitudinal surface) required by the process of negative variation, in order to transmit itself from the seat of excitation to the leading-off longitudinal contact. So too the *duration* of the negative variation may be calculated from the distance of the initial and final positions of the slider, and the revolutions of the wheel. We should expect the duration of the negative variation to increase with the distance between the leading-off contacts, and this obviously corresponds with a certain time-interval, which must be less in proportion as the tract between the electrodes is shortened. But this anticipation is not confirmed in experiment. The duration of the negative variation is approximately equal, whatever the distance of the contacts. This, however, means that the process which effects the backward swing of the magnet is demonstrated by the galvanometer only while it passes over the base points of the leading-off circuit in contact with the longitudinal surface, and not beyond these points. Bernstein gives the velocity of the negative varia-

tion at an average of 2.927 metres per sec. Its duration is $\frac{1}{250}$ to $\frac{1}{300}$ sec.

With the aid of this repeating method it is possible to decide the magnitude of the negative variation, and to determine whether at the moment when the curve of variation reaches its maximum, the current led off will sink to zero, or become reversed in direction. For this purpose the two mercury dishes are so arranged that the closure of the galvanometer circuit (T) is made as short as possible. Moreover, in experimenting, the slider must be placed in such a position that the closure of the galvanometer coincides after each stimulus with the maximum of the subsequent negative variation. When this is done, compensation may be shut off, and the first deflection on the galvanometer measured, as produced by the current in the non-excited muscle during the revolution of the rheotome wheel. Now, if the magnitude of the effect is determined during tetanus at the same rate of revolution, it will obviously depend on the difference in strength between "resting" muscle current and negative variation, in the interval under observation. The direction of the effect shows immediately which current is the strongest. If the current is reversed at the moment of the negative variation, i.e. at the time when it is at its maximum, the scale must turn in the negative direction. Bernstein, however, never found a negative deflection; the effect was always positive, although, as we should expect, it was much weaker than the corresponding deflection produced by the current in the resting muscle. As a rule, therefore, the curve of variation does not sink to zero.

The graphic record of these results is a great assistance towards understanding them, as was indeed anticipated in explaining the principle of the rheotome. Let (t , t') (Fig. 117) be the time abscissa, also two consecutive moments of stimulation, (h) the height of the resting muscle current, (T) the time of the galvanometer closure, supposed to be movable between (t) and (t'). If this occurs in (T') there will be no perceptible deflection, which first begins when the galvanometer closure occurs at T'' ; from that point the negative deflection decreases rapidly in magnitude with further alteration of the time of closure, and finally dies out (slowly), so that a curve is produced which falls steeply, and rises up again slowly, without, however (in the after-effect), recovering its original height. The deepest point of this

curve does not usually reach the abscissa (the muscle current is not abolished). The length (r, m) corresponds obviously to the period between the moment of excitation and the instant at which the process of the negative variation arrives at the first leading-off electrode, while the time represented by the line (m, o) corresponds with the period of the negative variation. In order to conceive the true process graphically, the figures must be imagined one behind the other many times over. While the stimuli follow at equal intervals (t, t^1, t^2 , etc.), the closure period (T) is always at the same distance from the corresponding moment of excitation; the effect on the galvanometer will then be zero. But if the closure of the galvanometer coincides with the beginning of the negative variation, the same impact will be repeated at

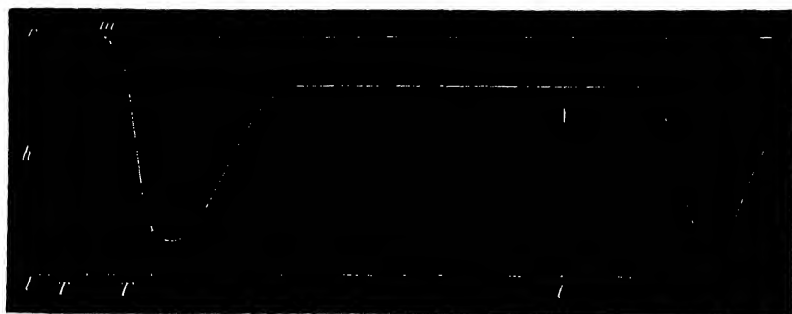


FIG. 117.—Schema of rheotome experiment. (Bernstein.)

each revolution, with a common effect on the magnet. This obviously resembles "that of a constant current, equal in height to the superficial content of all parts of the curves above (T), divided by the time of observation." It is possible in this way to construct the whole curve of variation from consecutive observations, and this has till now, at all events for striated muscle, been the sole means of determining its form and process. This would otherwise have been impossible without applying the method of summation (repetition), since even the most suitable instruments, *e.g.* the capillary electrometer, are incapable of adequately demonstrating the negative variation which corresponds with a single excitation. It is easy, on an aperiodic galvanometer with a very free magnet, to obtain a deflection from the negative variation that accompanies each single

twitch, but the time which such a deflection occupies corresponds much less closely with the time of the variation of current, than the movement of the capillary electrometer (which for the rest is far too insensitive for the object before us). Nevertheless, the construction of the curve of variation by a direct record is eminently desirable. Since it does not appear possible to overcome the sluggishness of the magnet, and to raise its mobility so far as to enable it to follow the quicker variations of the current faithfully, Hermann has recently tried the reverse method, by attempting to retard the galvanic process under observation as much as possible (21). He accomplished this by the simple and ingenious method of turning the two copper knobs, which effect contact with the galvanometer, and are attached to an ebonite disc, in the same direction as the wheel of the Bernstein rheotome during its revolution, only much more slowly. It is obvious that the interval between stimulus and galvanometer closure would thus be *constantly* altered, so that the whole process of the negative variation may be read off at a given reduction of time upon the galvanometer. The magnet would then follow the time-relations of the electrical change with complete fidelity, and it would only be necessary to transfer its movements by means of a ray of light reflected from the mirror on to a moving sensitive surface, in order to obtain a true photographic record of the curve of variation. It is superfluous to say that the results obtained by this method ("rheotachygraphy") coincide with the conclusions of the ordinary rheotome experiments.

The "variation curve" therefore corresponds with the development and time-relations of the negative variation in a definite part of the muscle, *i.e.* the point of the longitudinal section from which it is led off. But since the changes fundamental to it, which are unequivocally in direct ratio with the excitatory process, proceed *pari passu* with the rapidity at which excitation is propagated from section to section, it is legitimate to inquire in what length of muscle the single points are found after excitation to be *simultaneously* at different phases of negative variation. And thus we come to Bernstein's original proposition of the "*excitatory wave*" in muscle. "A muscle fibre (M, M) (Fig. 118) is led off from its artificial cross-section (q) and from the surface of the elements (d, M_1), which is hypothetically marked

off by two cross-sections in close juxtaposition. If the fibres in (p) are excited by momentary closure, the negative variation, after a given period, reaches the element (d, M_1) at the very moment at which the first signs of the negative variation appear in the galvanometer circuit. At the same moment, however, the negative variation reaches its maximum in the element (d, M_2) nearer to the point of excitation, while it has already subsided at (d, M_3), a third element.

"If the magnitudes of the negative variation are drawn as ordinates over these and the intermediate elements of the muscle-fibre, we obtain the curve (m, n, o), which represents the state of electromotive change in the subjacent elements of the muscle fibre." Bernstein designates the curve (m, n, o) the "wave of excitation." It spreads like an undulation from the spot

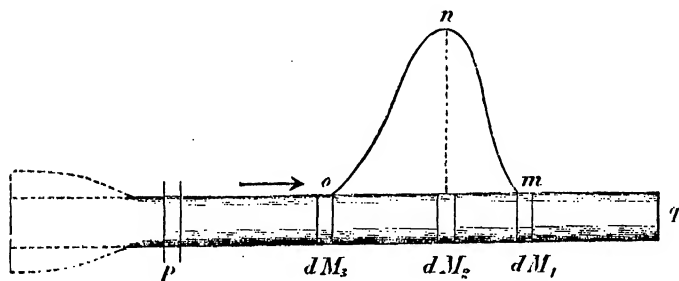


FIG. 118.—Schema of the "excitatory wave." (Bernstein.)

excited over the muscle fibre, in either direction, producing successively in each element of the fibre the complete process of the negative variation, so that the wave advances at its own length as long as the negative variation continues. Bernstein calculates the length of the wave at an average of 10 mm., from his observations.

If we sum up the results of all these experiments and discussions on the negative variation in a parallel-fibred muscle, provided with an artificial cross-section, it may be concluded that, if one end of the muscle is excited by single induction-shocks, while leading off from the other, a change is initiated in the first segment concerned at a given interval after each single stimulus, which interval corresponds with the distance between the leading-off longitudinal contact and the point of excitation. The change set up gradually increases, reaches its

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maximum at a certain moment, and is finally quelled again. These phases are expressed in the gradual reduction of difference in electrical potential between the two leading-off contacts in the muscle. Since we know that the artificial transverse section of the muscle is electrically negative towards each point of the uninjured surface, all these phenomena can easily be explained by postulating that *the change in the excitable substance propagated from the point of excitation through the muscle-fibres is associated with negativity of the latter*. We shall subsequently find direct proof of this dictum. For the moment it may be accepted as a hypothesis, which elucidates the foregoing observations. We assume, therefore, that at the moment at which a short stimulus (momentary excitation) takes effect upon any point of the fibre, a chemical alteration is developed at the same point, expressed by negativity of this part of the fibre towards adjacent, non-excited parts. Stress must be laid on the fact, as attested by every experiment, that this change (which must be regarded as identical with the excitatory process) begins directly at the moment of excitation, *i.e. without any perceptible latent period*, rapidly reaches a maximum, and then declines again slowly. The succession of the different stages of this change at the same point of the fibre, whether directly or indirectly excited, may be represented in a curve, designated above the "curve of variation." But since the process in question is not localised, but is, as a rule, transmitted with measurable velocity from the seat of excitation, over the entire fibre, a longer or shorter section of the muscle will always be found to be *simultaneously* (at different points) in different phases of negativity. If the values of these are erected as ordinates upon the muscle as abscissa, the resulting curve resembles in its form the curve of variation, and is called the "excitatory wave." Since the velocity with which the process of negativity (excitation) is transmitted in the muscle is known, as on the other hand the time at which the excitatory wave is propagated its entire length—this being identical with the duration of the negative variation at any definite point of the fibre,—the length of the excitatory wave may easily be calculated from the formula $s = ct = D$ (duration of negative variation) $\times V$ (velocity). Since the two values by which the length of the excitatory wave are determined differ in different muscles, and even in the same muscle at different times, the length of the

excitatory wave naturally varies considerably. Bernstein observed this, and Kühne, to whose experiments we shall return later, found that the velocity, and with it the length of the excitatory wave, varied considerably. In the most unfavourable cases the former was 25 cms. per sec., in other cases, on the contrary, more than 2 m. This recalls the striking fact that the same muscle may propagate slow and rapid waves of contraction, and we are in fact in both cases concerned with the same phenomenon, since there is nothing to hinder the identification of "excitatory wave" and "wave of excitation." It only remains, therefore, to establish the relations between this latter and the "wave of contraction." The fact that muscular contraction implies a latent period, which, according to Bernstein, is absent in the "excitatory wave," is *a priori* evidence that the "excitatory wave outruns the wave of contraction, partially at least, in an excited muscle fibre."

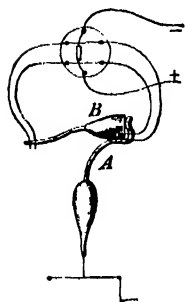


FIG. 119.—Period of negative variation. Helmholtz's experiment.

As early as 1854, indeed, Helmholtz stated that the negative variation, at any rate in its steepest part where the secondary twitch is excited, was the precursor of contraction. He located it at the middle, v. Bezold later on at the beginning, of the latent period. Helmholtz (22) arranged his experiment as follows:—The nerve *A* of a muscle (Fig. 119) connected with the writing-point of a myograph, bridged over the longitudinal and

transverse sections of the muscle *B*, the nerve of which was excited by a break induction shock, so that the negative variation of the muscle current of *B* produced secondary contraction in the muscle *A*. The measurable interval between the moment of exciting the primary preparation and the beginning of the secondary twitch of *A* was the sum of the four following time-values:—(i) interval between arrival of nerve excitation in *A* and beginning of contraction, *i.e.* latency period of *A*; (ii) interval corresponding with propagation of excitation in nerve of muscle *A*, from point of excitation to muscle; (iii) interval between arrival of excitation in *B*, and moment at which the negative variation excites nerve *A*; (iv) period of conductivity in nerve of *B*. By deducting the known intervals (found by other experiments), 1, 2, and 4 from the sum the required

magnitude 3 may be calculated, and is actually $\frac{1}{200}$ sec.; i.e. about $\frac{1}{200}$ sec. elapses between the moment of exciting the muscle and the moment of its most pronounced electrical variation. Starting with the length of the latent period, as originally assumed, at $\frac{1}{100}$ sec., the maximum of the negative variation coincides with the middle of the period of latent excitation. According to v. Bezold (23) the electrical variation begins, under its most favourable conditions, immediately after the moment of excitation, and therefore falls at the beginning of the latent period. The estimation of the latter has been constantly reduced since the time of Helmholtz, and Burdon-Sanderson has recently placed it much lower than Tigerstedt, who reckoned it at 0.005 sec. for frog's muscle. According to Burdon-Sanderson (24) the interval between excitation and the first sign of change of form is only $0.0025 = \frac{1}{400}$ sec., and since he allows an equally large latent period to the negative variation, there would thus be *no* perceptible interval between the two manifestations; whereas, according to Bernstein (*l.c.* p. 192), on the other hand, "each element of the muscle fibre completes its process of negative variation before it enters into the state of contraction." Since, however, on the one hand, the preoccurrence of the electrical variation can be directly observed in slowly contracting muscle, *e.g.* heart (*infra*), and, on the other, it appears on theoretical grounds to the last degree improbable that the excitation itself (*i.e.* changes in the contractile substance associated with negativity) should possess a latent period, the idea is confirmed that the beginning of the wave of excitation precedes the contraction wave, by however small an interval (*cf.* Engelmann, 25). This does not, of course, imply that it declines earlier in Bernstein's sense, or dies away at any particular point before contraction begins there, for while it is quite conceivable that a point of the muscle may be excited, and become negative to adjacent resting points without being perceptibly contracted, the contrary is impossible, and every contracted part must necessarily be assumed to be in a state of excitation also. In this sense, therefore, it may be said that *the electrical wave itself is an expression of contraction* (*cf.* Lee, 26). If, with Bernstein, we assume 0.015–0.023 secs. to be the latent period (which is not, in any case, conclusive), and start with the values calculated from this for length, duration, and

velocity of the excitatory wave, then on exciting a muscle at any given point the excitatory wave would already, after the period of latent excitation, have traversed a tract of 45–92 mm. in the fibres, before contraction began at the seat of excitation. Moreover, the vast difference that exists, according to Bernstein, in the length of the two waves, would also come into consideration. While the excitatory wave is about 10 mm. long, the wave of contraction ranges between 198 and 380 mm. This last statement, however, needs consideration when it is recognised that each contracted fibre point must be regarded as “excited,” and on the other hand admitted that negativity is the galvanic expression of excitation. The first assumption is essentially restricted by the fact that in all recent experiments the latent period is found to be much shorter than was formerly supposed. Moreover, F. S. Lee (*l.c.*) has recently, by means of the capillary electrometer, found considerably higher values for the duration of the wave of excitation than any previous observer, so that no doubt remains that, at least in fresh muscle, “electrical differences of potential, which are associated with contraction, are demonstrable for a much longer period than had previously been concluded.” This also agrees with the idea that the electrical wave falls in the latent period of the contraction, and (as a whole) outlasts it (F. S. Lee). The values found by Lee for the duration of the wave of excitation are in fact of the same order as the duration of the contraction (0.05–0.26 secs.)

It thus appears as though du Bois-Reymond’s interpretation of the secondary contraction was after all the only adequate and possible conclusion—since it was shown that with each single excitation the demarcation current of a muscle underwent a very rapid negative variation, which could be excited by a nerve bridging over the longitudinal and transverse section, provided the preparation were sufficiently excitable. This explanation necessarily underwent considerable modification when the justice of Matteucci’s original contention was established, viz. that the appearance of the secondary contraction is independent of the position of the nerve on the primary muscle, since “parelectronic” gastrocnemii, when excited from the nerve, were also able to excite a secondary preparation, the nerve of which bridged the longitudinal and natural transverse

sections of the primary muscle, or was merely in contact with the latter. It is obvious that we cannot here speak *a priori* of a negative variation, since the current which should vary is absent, at least as regards any branch that can be led off to the galvanometer. It is therefore imperative to investigate the galvanic effects of excitation in the uninjured, currentless muscle. But before we enter upon the complicated relations of indirect excitation of the gastrocnemius it is advisable to examine the simplest case of direct excitation of the currentless sartorius.

If one end of the muscle is tetanised while leading off at the other end from the natural cross-section and a point on the longitudinal surface at about the middle of the muscle, a current appears, as du Bois-Reymond found, during excitation, in the direction of a negative variation, even where no trace of a regular muscle current had previously been present, inasmuch as the tendon end is positive towards every point of the longitudinal surface. We must adopt Hermann's designation of this as the "action current" because, independent of the presence or absence of a current of rest, it characterises the active state of the muscle. As a corollary to Hermann's view, the negative variation of the demarcation current was explained above as signifying that the contractile substance under the electrode in contact with the longitudinal surface becomes more or less negative at the instant when a wave of excitation, or "excitatory wave," passes under it, when the original difference of potential between longitudinal and artificial transverse section is of course diminished in proportion. But it is evident that the same canon of interpretation cannot be *prima facie* applied to the present case of uninjured, and therefore currentless, muscle. For if we are to assume that the normal ends of fibres, like all other parts of the muscle, take part in the excitation (and there is no evidence to the contrary), they must, when the excitatory wave reaches them, become as negative as every preceding segment. Then, however, under the given conditions, a descending current directed in the muscle from longitudinal section to tendon could not appear during tetanisation, much rather would the absence of current, obtaining before the excitation, continue also during stimulation. Later on, Hermann's theory will be found to give a simple solution of this

apparent contradiction, while du Bois-Reymond (whose interpretation of the negative variation in the muscle current will be discussed below) finds himself reduced to the highly improbable assumption that the natural, uninjured ends of fibres, or parelectronic layer of the same, take little or no part in the excitatory process.

Against this, it must be remarked in the first place that a tetanic action current in the same direction may always be observed when the ends of fibres are not included in the leading-off tract, any two points in the longitudinal surface of the muscle being taken as the contacts of the leading-off

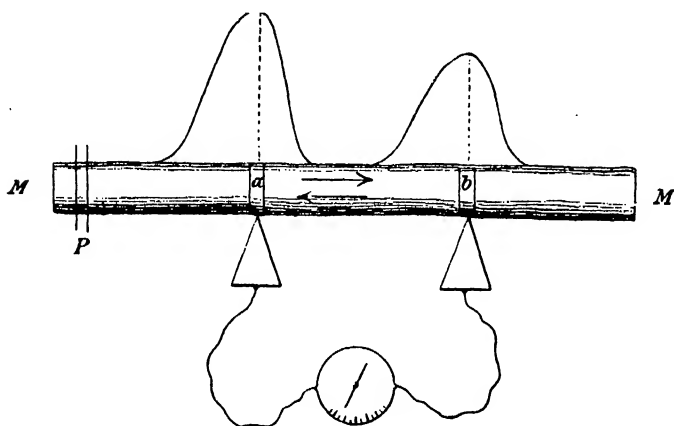


FIG. 120.—Schema of the diphasic action current. (Bernstein.)

circuit (Hermann, 27). The cause of this may be determined by an experiment first carried out by Bernstein (*l.c.* p. 160 ff.) with the aid of the rheotome; it is also valuable in other connections.

Let (M , M) be a regular muscle with parallel fibres, at one end of which single stimuli are led in at equal intervals by the rheotome (Fig. 120), while between every two excitations there is a very brief closure of the galvanometer circuit at any convenient moment of the pause between the excitations; then—if excitation and galvanometer closure occur simultaneously—no result can follow, since the wave of excitation, starting from (P), requires a certain time to reach the nearest leading-off point (a). But if the galvanometer circuit is always closed at

the moment at which the beginning of the excitatory wave has reached the point named, *i.e.* so long after each individual stimulus as the wave requires in order to travel over the distance (P, a), a perceptible deflection of the magnet may be expected in the sense that (a) will be negative to the second led-off point (b), if it is correct that each point under the excitatory wave is negative to each point beyond it. If the closure of the galvanometer circuit is advanced still further in the same direction, so that other superficial points of the curve of variation are excluded, the effects must at first increase in the same direction, reach a maximum when the excitatory wave is at its acme, and finally decline to zero when the entire wave of excitation has passed the point (a). Starting from Bernstein's computation of 10 mm. for the length of the wave, with the two leading-off electrodes at more than 10 mm. from each other, the end of the excitatory wave will have passed the point (a) before the first part reaches (b), and the same still obtains a little later, provided the electrodes are sufficiently far apart. At a certain adjustment of the rheotone slider, corresponding with this interval, there will therefore be hardly any difference in potential between (a) and (b). It is not till the closure of the galvanometer circuit is so delayed after each single stimulus that the first part of the excitatory wave has already reached the point (b) that there will again be any marked deflection, and that in a direction *diametrically opposite* to the earlier variation, since (b) is now negative to (a). The difference in potential increases as before with further advancement of the galvanometer closure, attains a maximum, and finally, when the end of the excitatory wave has passed under (b), declines to zero. Thus, on leading-off from two symmetrical longitudinal points of a muscle, rhythmically excited (tetanised) by induction shocks, there is, after each single stimulus, a double variation, or, more properly, a *diphasic current of action*. Bernstein, to whom we owe the discovery of this fact, named the current which appears while the wave of excitation is passing under the point a , and has the direction of the lower arrow in the muscle (Fig. 120), the *negative variation*, that which follows it in the direction of the upper arrow, the *positive variation*. It is evident that the absolute magnitude of the deflection produced by the first action current should be

exactly parallel with that derived from the second; but according to Bernstein this never is the case, *the positive being always smaller than the negative variation*. Accordingly, the excitatory wave decreases in amplitude as it is propagated along the muscle-fibres; in other words (at least in excised muscle), it is decremental. The double action current observed after each single excitation in uninjured, currentless muscle may be termed, after Hermann (27), the "phasic current of action." The first phase is directed from, the second towards the seat of excitation. If one of the leading-off contacts is applied to an artificial cross-section, the corresponding phase will make its appearance. Since the galvanometer magnet is much too insensitive to respond by corresponding deflections to these opposite currents (which follow with extraordinary rapidity in tetanising excitation), we should anticipate that on leading off without current from two points of the longitudinal section, there would be no effect even during tetanus. That this is actually not the case may be explained from the fact that the excitatory wave decreases in amplitude during its transmission through the muscle; it follows directly that on leading off from two longitudinal points of an uninjured, currentless, parallel-fibred muscle, a difference in electrical potential must appear between the two points, when one end is tetanised by an ordinary induction coil: the longitudinal contact proximal to the seat of excitation must always be negative to the distal point, since the latter, owing to the decrement of the excitatory wave, must always be less negative than (*i.e.* relatively positive to) the former. Such an action current is in fact present in tetanus, and has been confirmed by du Bois-Reymond and Hermann. The latter found the E.M.F. of this current, which he described, from reasons given above, as the "decremental action current of tetanus," to be of considerable proportions (0.002–0.02 Dan.) Du Bois-Reymond originally believed that decremental action currents were only to be observed on fatigued, moribund muscle, *i.e.* that the excitatory wave only diminished in these cases. Hermann, however, showed that the decrement obtains immediately after making the preparation. Since the excitatory wave becomes smaller in proportion as it is further from the seat of excitation, the individual transverse sections of a muscle tetanised at one end

must be the less negative, the nearer they lie to the end not excited. Hermann gave direct proof of this by leading off from a number of loops of thread, placed round a regular muscle with parallel fibres; one end of the muscle was tetanised, and the E.M.F. of the action current determined between each pair of contacts. He found it "approximately proportional to the relative distance of the loops and quite independent of their position." "Each point traversed by the excitation is thus, during tetanus, the seat of electromotive force, homodromous with the wave of excitation." And thus it appears that the "negative variation" in its original manifestation is no more than a special case of the action current in tetanus, in which the reciprocal phases ensue on leading off from an artificial transverse section.

Since under normal conditions the muscle is always excited indirectly, *i.e.* from the nerve, a special interest attaches to the investigation of the action current in uninjured muscle with this kind of excitation; the more so as all the earlier experiments on the negative variation were made, from motives of convenience, with what is intrinsically the least suitable object—the frog's gastrocnemius tetanised through its nerve. The same uninjured muscle was also the subject of the first series of exact analytical experiments made on the action current, with indirect excitation, and led off from the two tendinous ends by Sigmund Mayer (28) under Bernstein's direction, and with his rheotome. The complicated manifestations observed (accounted for by every possible interpretation and explanation) first became intelligible when Hermann, in 1877, began to investigate the action current of regularly constructed parallel-fibred muscles, with indirect excitation. With our present knowledge of the relations between nerve and muscle it is legitimate to assume that the excitation is discharged at a definite point in every muscle-fibre, on stimulating the nerve fibre belonging to it, *i.e.* at the nerve end-plate, which is situated between the contractile substance of which it is the continuation, and the nerve-fibre of which it is the conducting organ. We shall presently have to examine the histological and physiological relations between nerve and muscle in detail; for the moment it is enough to say that it has been ascertained that the nerve-fibre is connected with only a limited tract of the muscle-fibre or fibres belonging to it, which by no means prevents the same muscle-fibre from

being served *at different points* by a plurality of nerve-fibres. The theory that has recently found much support, from J. Gerlach in particular, to the effect that there is no proper nerve-ending in muscle, since the nerve as it enters passes over the contractile substance in the whole extension of the muscle, ramifying everywhere between the elements of the muscle-fibre, in the form of the finest varicose fibrils, must now be regarded as refuted, the more so since it has been shown that Gerlach's nerve-fibrils are really no more than the darkly-stained (gold chloride), and therefore strongly-reducing, interfibrillar substance (sarcoplasm) of the muscle. If the excitation thus starts, with indirect stimulation, from the points of the fibre corresponding with the nerve-ending, it must necessarily be transplanted thence in an undulatory form on either side through the fibre. This is no mere theoretical conclusion, but receives direct confirmation both from histological investigation and from physiological experiment. As regards the former, weighty evidence has recently been contributed by Föttinger, Rollett, and others to the effect that the "fixed wave of contraction"—which is easily demonstrated in the muscle-fibres of many insects, after proper treatment of the living tissue with hardening and preserving fluids—obtains mainly at the point where the nerve enters, so much so indeed that the maximum of contraction, *i.e.* the crest of the wave, usually falls in the centre (sole) of Doyer's expansion. This, in addition to direct observation of still living fibres, shows unequivocally that the entrance of the nerve is the starting-point of an undulatory contraction propagated on either side through the muscle.

The advance of the negative wave of excitation is demonstrated with equal precision in the galvanometer, on indirect excitation of the entire muscle, thus obviating the doubt expressed by du Bois-Reymond as to the undulatory nature of excitation, when the muscle is stimulated from its nerve. The adductor magnus of the frog is in all respects a suitable preparation, the nerve entering by the centre of the muscle; this muscle is a little more troublesome to prepare than the usual gastrocnemius and sciatic nerve-muscle preparation, but the regularity and certainty of its results are ample compensation. We may assume from the previous experiments that such a preparation, on the excitation of its nerve by induction shocks, will respond exactly like the muscle excited directly at the nerve end-plate, in special cases, *i.e.*, at the

centre. Hence it is a great advantage to lead off, in indirect excitation, from the actual seat of the excitatory process. If each nerve-ending lay exactly in the middle of the corresponding fibre of the parallel-fibred muscle, a negative wave of excitation, or contraction, would obviously be propagated from it in both directions through the muscle at the moment of excitation. Then, on leading off from the middle and tendon end of such a muscle to the galvanometer, while single shocks were sent into the nerve at equal intervals by a Bernstein rheotome, a diphasic action current would be demonstrable, consisting of a first "atterminal (abnerval)," and a second "abterminal (adnerval)" phase. Such a response was actually found by Hermann in his experiments with the sartorius preparation. Both halves of the muscle at first indicated an atterminal current directed from the centre to each tendon end, while a little later, *i.e.* at the interval required by the excitatory wave to traverse the muscle from centre to tendon end, an abterminal action current appeared, which, owing to the decrement of the exciting wave, was always weaker than the first current. On leading off from both tendon ends, we have at each moment the algebraic sum of the effects in either half; this sum of course = 0 in a properly symmetrical muscle, in others its sign varies with the time-interval. These experiments of Hermann give physiological proof of the undulatory course of excitation in indirect stimulation, and we may now proceed to consider the action current in its more complicated examples, with indirect excitation of the gastrocnemius. S. Mayer (*l.c.*) found first a descending and then an ascending action current, on leading off from both tendinous ends of this muscle, after each single excitation; or, as it was then expressed—because the first current was identified with the negative variation of the muscle corroded at the achilles expansion—a variation first negative and then positive appeared, a fact confirmed later by du Bois-Reymond with Bernstein's rheotome, which S. Mayer had also employed, and by Hermann with the (non-repeating) "fall-rheotome" described above. If the tendo achilles was corroded, the ascending (positive) half of the current was absent. Holmgren (29), moreover, by means of a light magnet (without rheotome), had frequently observed, before Mayer, a diphasic variation on the gastrocnemius, as well as cases of simple positive, and negative variations. According to Hermann the gastrocnemius may be regarded, diagrammatically, as

a muscle rhombus, and it is tolerably accurate to say that the nerve-ending lies in the middle of each fibre (Fig. 121). But then it follows that all the points corresponding with the upper contacts (*a*, *b*), i.e. the thick part of the muscle, must be affected more, and earlier, by the waves of excitation from the nerve-endings (*a*, *β*) than the lower ends of fibres, corresponding with the tendo achilles. Thus there will at first be a descending, and subsequently a weaker ascending, current of action. "The upper half of the muscle, on the contrary, should vary first in an ascending and then in a descending direction; here, however, the structure of the muscle is essentially different; the main part of the current ('*Neigungstrom*') is prevented by the folds of the upper



FIG. 121.

expansion from producing any external effect, so that in the first place the abterminal phase of the upper half of the muscle is hardly perceptible, and in the second the upper tendon as a whole must be regarded as a lead-off from the longitudinal section. On leading off from both tendons, the effects are consequently not very dissimilar to those with the lead-off from belly and achilles tendon. There is thus no doubt that the first descending phase starts, not from the expansion of the tendo achilles, but from the

longitudinal section, while the second ascending phase does originate at the achilles expansion" (Hermann). With the corrosion of the latter, the second phase naturally dies out, since the ends of fibres then become negative without it. And this of course applies to tetanus, in which du Bois-Reymond first observed the descending effect in the currentless gastrocnemius, since, generally speaking, only the algebraic sum of the opposed action currents can be detected. But, owing to the preponderance of the first descending phase, the effect is actually descending. It is unnecessary here to enter into further minutiae of electromotive action in the excited gastrocnemius, since no new theoretical data can be expected from it. We need only mention that Matthias (30) has recently (by Hermann's "rheo-

tachygraphic" method, as described above) published a *graphic* record of the gastrocnemius action current, which, on leading off from the tendo achilles and from a point proximal to the nervous equator, gives double-topped curves, in which the first descending phase is succeeded by a second, weaker, ascending variation, after which the magnet returns to its zero with some insignificant deflections (Fig. 122).

This dissimilarity is apparently due to a partial superposition of the two phases; the excitation has not entirely passed the upper lead-off before it reaches the lower. The gastrocnemius curve of electrical variation is even more complicated on leading off from the centre and tendo achilles, as in the observations of Lee which we have frequently referred to, in which the more sluggish galvanometer is replaced by the sensitive capillary electrometer. The rheotome method can also be applied here. The curve (Fig. 123, *a*) corresponds with a triphasic variation, its two negative sections being separated by a double-topped, positive, and very steep segment. The duration of the entire process amounts to 0.26 sec., a value which we have seen to be approximately equivalent to the duration of a twitch in the muscle. The wave of variation in the sartorius, on the other hand (when led off from the middle and end of the muscle), was found by Lee to be *diphasic*, no conspicuous decrement being visible in the fresh, uninjured muscle. Both sections exhibited a tolerably symmetrical figure (Fig. 123, *b*). If, however, the tendon end of the muscle is injured ever so slightly, the first ("negative") phase prevails, and the second may disappear entirely, as shown by the lower curve of the same figure. In this case the variation, which is now monophasic, does not appear perceptibly shorter than the sum of the two earlier phases, which again implies superposition of the two components. The triphasic wave of the gastrocnemius again (in progressive fatigue, or injury, of the lower end of the muscle) undergoes alteration in the sense that the middle positive section disappears, or is merely indicated. For the rest, the fatigue changes in the curve of electrical variation in striated



FIG. 122.

muscle have a special interest, inasmuch as they once more illustrate the intimate relations (*supra*) which exist between the current of action and the phenomena of contraction. According to Lee, the curve of the former alters in the same sense as that of the twitch, since on the one hand it decreases in height by the reduction of all its ordinates, while on the other its time-relations are more extended.

We have seen that all electromotive manifestations in

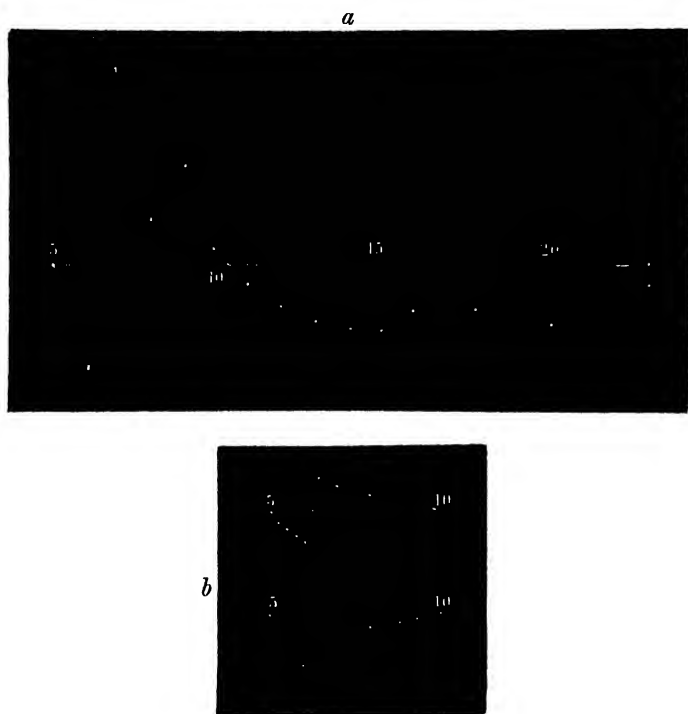


FIG. 123.—*a*, Triphasic curve of variation in gastrocnemius muscle; *b*, biphasic curve of variation of sartorius muscle. Above is the normal, below the injured, muscle. (F. S. Lee.)

isolated muscle, with direct or indirect excitation, may be easily explained without further hypothesis by Hermann's alteration theory, on the simple assumption that *excited fibres, like moribund fibres, are electro-negative to normal or resting fibres*. The fundamental data of this theory render such a proposition self-evident, since in both cases there is, in Hering's sense, a descending alteration of the living matter, so that action

current and rest current must alike be referred to the same cause, "since both are to be regarded as the external symptom of a different ratio of descending change in the two parts of the muscle brought together in the circuit." Accordingly, there is as little essential difference between action current and rest current, as between excited and dying muscle-substance. From this point of view it is meaningless to ask whether the "potassium current" in muscle (as above) is, or is not, to be regarded as an action current. The circumstance that it appears in etherised muscle proves as little against the former assumption as the presence of the normal demarcation current, under the same conditions, against the latter.

From the standpoint of the molecular theory, the electromotive response of uninjured, currentless muscle encounters great difficulties of interpretation, which can only be met by supplementary hypothesis. It is superfluous to enter on the detailed discussion of these, since they are based on the palelectronic theory, the invalidity of which can hardly be disputed. A brief exposition of the fundamental canon by which du Bois-Reymond interpreted the negative variation of the demarcation current is all that is required. He derives it essentially from a diminution of E.M.F. in the "molecules," or from their rearrangement in a form less centrifugally active. Bernstein's new "electrochemical theory" also postulates a "decrement of charge in the molecules," from which he explains the negativity of each point excited. "If the excitatory wave is propagated to the cross-section, the charges of the molecules also decrease *pari passu*. When the wave reaches the cross-section it fails to produce any current in the opposite direction, *i.e.* second positive phase of variation, because the charges of the molecules are always the same on the side towards the cross-section." In order to explain the electromotive action of currentless muscle, du Bois-Reymond is forced into the hypothesis that the palelectronic layer, or tract, at the natural cross-section takes little or no part in the negative variation, while, according to Bernstein, the uninjured ends of fibres react like any other longitudinal points. Du Bois-Reymond believed that the breaking of the excitatory wave upon the natural cross-section was the direct cause of palelectronomy, since he held that this was favourable to the development of the palelectronic molecules.

From all this we may surely conclude in favour of the greater simplicity of Hermann's alteration theory, the more so since, as we shall see in the sequel, it brings under the same comprehensive point of view those electromotive reactions in living tissues (gland currents and vegetable currents), which have hitherto defied the molecular theory. Finally, it is elevated above the rank of an arbitrary hypothesis adjusted to the facts, by a series of experimental researches, which leave no doubt as to the justice of its fundamental conception.

In addition to all the evidence above quoted, *re* "rest current" and action current in the muscle (in respect of which the alteration theory is luminous), a few data remain, which are best subjoined in this connection. Foremost among these is the *electromotive reaction of the so-called idio-muscular contraction*. We know that in moribund muscle, especially in warm-blooded animals, conductivity disappears much earlier than excitability. The contractile substance, as Funke expresses it, acquires more and more the properties of a viscous mass, which tends to retain the local impression instead of propagating it. Eventually, with localised excitation, a merely local contraction results in the fibres, and is usually persistent. Hence, as it were, a fixed wave of contraction arises, extending over a greater or lesser section of the fibres. The local persistent contraction must, however, correspond with localised persistent excitation, and this again induces negativity towards normal points of fibres. As early as 1857, *i.e.* ten years before the formulation of the alteration theory, Czermak gave proof that when the prepared nerve of a frog falls on a muscle with an idio-muscular swelling, so as to bridge the latter and a normal longitudinal point, a twitch ensues, thus demonstrating a P.D. between the swelling on the one hand and the uninjured surface on the other. Later investigations of Kühne and Harless prove that the swelling is invariably negative towards all other points of fibre.

We have observed repeatedly (Biedermann, 16) that negative zones may be present also in the continuity of the frog's sartorius. These are due to partial persistent contraction of the otherwise uninjured muscle, and sometimes give rise to very powerful currents. It is obvious that this may simulate the effect of a parelectronic layer of measurable dimensions (parelectronic tract) at the uninjured ends of the fibre, since it is conceivable in

such a case that superficial corrosion of the natural cross-section proximal to the tendon might not immediately develop a normal current, if the negativity of the leading-off contact of the longitudinal section is equal to, or greater than, that of the artificial cross-section at the end of the muscle. Such a wave of contraction is easily produced at any given point of a muscle with parallel fibres by the local application of veratrin solution, which, of course, retards the decline of the excitation very considerably. Hermann obtained the same result by energetic cooling of the muscle. And lastly, if it counts as the touchstone of a theory that new facts can be predicted upon its basis, the "secondary electromotive manifestations" must be cited, to which we shall return later.

After it had been ascertained from experiments on isolated muscles that the state of activity is accompanied by electromotive alterations demonstrable on the galvanometer, it became a desideratum to establish the same for uninjured muscle *in situ*, in man and other warm-blooded animals. Du Bois-Reymond accordingly, with admirable perseverance, carried out a research which is a pattern of sustained and deliberate investigation. If his attempts to discover differences of potential—in the sense of a "resting muscle current"—through the skin of the intact frog were frustrated by the strong electromotivity of the skin itself, the experiment was no less difficult on the human subject. But we need not dwell on the point, since there now appears as little reason for ascribing demonstrable electromotive activity to human muscles during rest, as to those of the frog or any other animal. On the other hand, du Bois-Reymond's attempts to demonstrate currents that could be led off externally during voluntary contraction, or, in the language of his theory, the negative variation of the pre-existent muscle current, were crowned with success.

His classical experiment, which, when first published, created an enormous interest, is arranged as follows: One or more fingers (preferably the forefingers) of each hand dip into the vessels of conducting fluid, which again are conveniently connected with the terminals of the galvanometer or multiplier circuit (Fig. 124). When the magnet has come to rest under the influence of the natural (and usually insignificant) current which results from inequalities in the two points of the skin from which the current is led off, a sharp contraction of the muscles of one arm generally

causes an effect in the direction of an ascending current in the arm, which, according to the later measurements of Hermann, has a very low potential (0.0014–0.0023 Dan.) An analogous result is obtained on leading off from both feet. In order that the experiment may succeed it is essential that the voluntary muscular action should be as vigorous as possible. Du Bois-Reymond strained his arm until “the muscles appeared as hard as boards, the arm shook violently, and after some seconds a lively sensation of warmth was experienced.” Sometimes, as

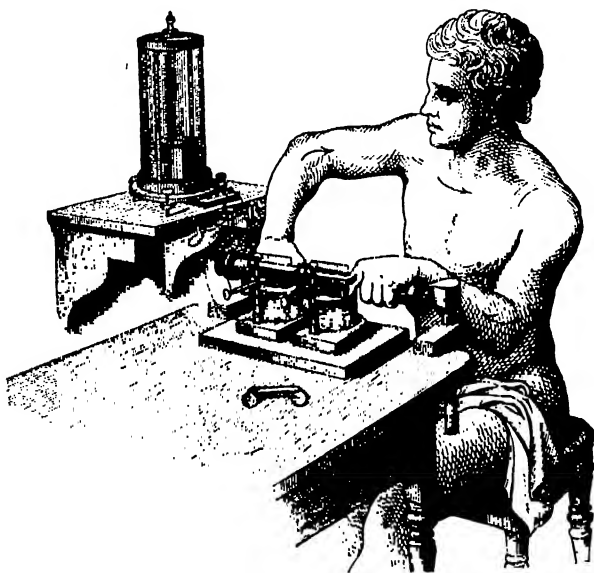


FIG. 124.—Du Bois' "voluntary experiment." (Du Bois-Reymond.)

proposed by Mousson, a battery was formed by the co-operation of several persons, a vessel of concentrated salt solution being placed between two, into which each person dipped a finger, and simultaneously stretched one arm (on the same side). All these galvanic manifestations were characterised by a long after-effect, as well as by inability to evoke secondary excitation in the physiological rheoscope, to which we shall return later. This fact in itself is in no way prejudicial to du Bois-Reymond's dictum that the effect under discussion is the expression of the negative variation of the muscle current in the human limb.

On the other hand, various other considerations have been

brought forward, which relate partly to the direction of the current observed, partly to the possibility of referring it to changes of temperature in the muscle, or electromotive action in the skin, however originated. As regards the first point, the contradiction was emphasised between the descending effect in muscular contraction of the frog's leg, and the ascending current in the arm (or foot) of the human subject. Du Bois-Reymond indeed found that a P.D. did exist in the skinless leg of the rabbit in the sense of a descending "rest current," with a corresponding ascending negative variation. With regard to Hermann's theory as applied to the currents of groups of muscles, *i.e.* whole extremities, neither the above objection, nor du Bois' proof of the corresponding variation in the leg of the rabbit, need detain us. On the other hand, in the commission appointed by the Paris Academy to inquire into du Bois-Reymond's experiments on man, the elder Bequerel did raise an objection against his interpretation, which we must examine more closely, since in spite of du Bois Reymond's objection it has subsequently been thoroughly substantiated.

According to Bequerel, voluntary tetanus of the arm produces increased secretion from the skin of the finger, in consequence of which the electromotive properties of the skin itself may undergo alteration. And when du Bois-Reymond himself, at Bequerel's request, dipped the forefingers of both hands into the leading-in vessels, after voluntarily contracting and relaxing one arm, there was in fact "a weak effect in the same direction as if the arm belonging to the immersed finger had been contracted"; but this was referred to the prolonged after-effect (*supra*) of the supposed negative variation. Du Bois considered the following experiment to be conclusive in favour of his interpretation. The hand and lower part of the arm were confined in a gutta-percha bag, bound to the arm below the elbow, to produce local perspiration. The same parts were further bound with a woollen cloth. After some time the perspiring arm was compared with the normal limb by the usual galvanometric method, on which it appeared that the former was not, as might have been expected from Bequerel's theory, negative, but, on the contrary, positive to the latter. That, notwithstanding, there was in du Bois-Reymond's voluntary experiment nothing more than the effect of a secretion current, was first ascertained at a

much later period by Hermann, to whom we are indebted for the first proof of true galvanic muscular effects produced in the living human subject by the current of action. In supplementing his investigations on the action current in frog muscles, Hermann endeavoured in the first place to demonstrate on a *single* convenient group of muscles the anticipated decremental current of action in tetanus. For this purpose he selected the forearm, leading off from the thick part of the flesh, and from the proximity of the wrist, by appropriate electrodes. These electrodes consisted of thick ropes, saturated with ZnSO_4 , looped round the parts of the arm as above. Yet the expected (descending) current failed to appear here, as in corresponding experiments on the thigh; only small and irregular deflections were visible. It thus seemed questionable whether, under the conditions described, there was any development of a decremental action current in human muscle during voluntary excitation. Hermann in consequence applied himself, with far greater result, to the task of investigating the phasic action current under the same conditions, but with artificial excitation from the nerve (27). As was stated above, a diphasic current may be demonstrated by means of the rheotome method, between every two points of an uninjured muscle, directly or in-

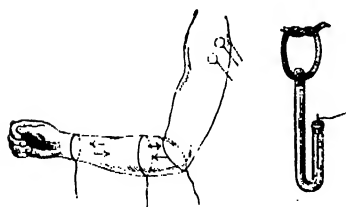


FIG. 125.—Diphasic action current in the human forearm. On the right, an unipolarisable rope electrode.

directly excited, the first phase being abnerval, the second adnerval, in direction. In consequence of the decrement of the excitatory wave in excised muscle, the second phase is distinctly weaker than the first. The arrangement of the experiment is shown in Fig. 125, after Hermann.

The stimuli must be so strong that vigorous twitches ensue in the muscles of the forearm. The results, which consisted in the appearance of a diphasic action current, at first descending (atterminal), and subsequently ascending (abterminal), were so regular that Hermann was able to denote this experiment as one of the most certain in electro-physiology, "giving, without exception, better and more extensive results in man than in the frog." The same results were obtained on leading off from the

upper muscles of the forearm also, as described in Fig. 125, *i.e.* once more, in the direction of the arrows, first an atterminal (this time ascending), and then an abterminal (descending), phase of the action current.

The "nervous equator," *i.e.* that section of the muscle "in which would fall the common centre of gravity of all the nerve-endings, if these last have a certain uniform equilibrium," lies, in the human forearm, pretty close to the elbow. *The approximate equality of both phases* is remarkable, from which it may be concluded "that a decrement of the excitatory wave does not exist in the intact muscle with normal circulation," and this at once explains why the action current fails to appear with any certainty on tetanising without the rheotome. Hence the ascending current observed by du Bois-Reymond in voluntary innervation of the arm and leg is no current of action from the muscle. That it is a "secretion current" caused by the activity of the skin-glands in the sense of Bequerel's original presumption, follows directly from the experiments of Hermann and Luchsinger, to be discussed below. The results obtained by du Bois-Reymond on leading off simultaneously from a perspiring and a dry hand, upon which the former shows a descending current, cannot be recognised as a valid objection, since they depend not so much upon the secretion present as upon the *secretory process* caused by excitation of the nerve. Like Bernstein's experiments on the negative variation, or current of action, in frog's muscle, the experiments of Hermann on the human forearm give the requisite opportunity for determining the velocity of excitation in normal human muscle. Its most probable value is 10-13 m. per sec.

Matthias (30) has recently published a graphic record of the action current in the human forearm, obtained by Hermann's "rheotachygraphic" method.

Smooth muscles, owing to the much slower period of all excitation phenomena, are in many respects more suited to the investigation of the action current than striated muscles, which have hitherto been almost exclusively investigated. It is evident that where the wave of contraction is as prolonged as, *e.g.*, in the rabbit's ureter, the phasic action current will be directly demonstrable in a sensitive galvanometer without applying to the repeating method. In the last resort, however, the number of objects

which can be used is unfortunately limited, chiefly because a locally discharged excitation remains localised in most smooth muscular organs, and is not propagated further. Cardiac muscle, on the other hand, the physiological properties of which entitle it to some extent to a middle place between striated muscle and smooth muscle-cells, presents an object peculiarly appropriate to the investigation of galvanic phenomena. As early as 1855 Köl liker and H. Müller (31) observed the negative variation on spontaneous contraction of a frog's heart provided with an artificial cross-section, by means of the multiplier; they soon discovered that secondary contraction may also be obtained from the same preparation, if the nerve of a rheoscopic limb is properly bridged across the longitudinal and transverse sections. Each systole is followed by a twitch in the leg, occurring after the auricular, and almost imperceptibly before the ventricular, systole. "The twitch took effect sometimes in the lower part of the leg, sometimes at the tarsus and toes, and was visible throughout as a single transitory contraction" (*l.c.* p. 99).

It was presently found that the same experiment produced results in the intact heart also, even when the secondary nerve was laid transversely across the middle of the anterior surface of the ventricle. The surface of the uninjured heart being isoelectric (as was shown above), this last observation on currentless cardiac muscle shows once more that the interpretation of secondary contraction as a consequence of negative variation, as given by du Bois, is not justified, but that the electromotive effects (current of action) associated with the activity of the muscle must have acted as a discharging stimulus to the nerve lying upon it. The facts discovered by Köl liker and Müller were subsequently confirmed and extended by Meissner and Cohn (32). Donders (33) repeated the experiment on secondary excitation from the heart with the aid of the graphic method. He recorded simultaneously in dog and rabbit the heart-beats and the contractions of a frog's leg, the nerve of which rested on the heart. As a rule each systole discharged a simple twitch in the leg. Donders found, like Köl liker and Müller before him, that the simple systole was invariably followed by a secondary double contraction. It was always possible to demonstrate that *the secondary twitch appeared earlier than the primary heart contraction* (about $\frac{1}{10}$ sec. in rabbit). In a recently killed dog, whose

right ventricle was still beating feebly, the time-difference was $\frac{1}{17}$ sec. The same was demonstrated again by Nuël on the frog's heart. On the dog he was able, by the physiological rheoscope, to demonstrate that the contraction of the auricle is accompanied by as marked an electromotive variation as that of the ventricle, and that the time-difference between the two electromotive processes corresponds entirely with the contraction of the two cardiac sections.

In order to ascertain more exactly the time-relations and form of the electromotive variation (the "excitatory wave") which accompanies activity in cardiac muscle, experiments were undertaken almost at the same time by Engelmann (34) and Marchand (35) on the frog's heart, with Bernstein's rheotome. The ventricle, which had been quieted by the removal of the auricle, was stimulated either at its base or apex by a single induction shock; whatever the situation of the lead-off from the surface of the ventricle, or the alterations in its length, and distance from the point of stimulation, the first effect was invariably a current directed in the heart away from the seat of excitation. The rheotome is indeed superfluous in this connection. The galvanometer circuit may be permanently closed; with a sufficient length of tract led off, and moderate sensitivity of galvanometer, the first effect of the stimulus in every case is a deflection of the scale in the given direction. Accordingly, each portion of the ventricular muscle must, during excitation, become temporarily electromotive in a negative direction, which negativity (as also contraction, according to Engelmann) is propagated from the seat of excitation, wherever this is situated, in all directions through the ventricle. With the rheotome it may further be shown that on leading off from the external surface of the ventricle by two points that give no current during rest, and are at unequal distances from the seat of excitation, the electromotive response of the heart corresponds as a rule with that of normal, striated, parallel-fibred muscle led off from two longitudinal surfaces; *i.e.* a diphasic variation usually makes its appearance, and that of such a kind that the point nearest to the seat of excitation is at first negative, and then positive, to the more distant point (Fig. 126).

In an equal number of cases, however, the second (positive) phase is wanting, and either the initial state of indifference

of the heart-muscle. It is evident that these facts coincide with Hermann's theory, according to which a point of the muscle must remain negative as long as the excitatory (or contraction) process continues. Accordingly, we should expect the surface of the ventricle to be isoelectric during the period of systolic contraction, as actually appears from the experiments of Burdon-Sanderson and Page.



If, in the accompanying Fig. 127, (*a*, *x*) is the spot excited, (*F'*) and (*m*) the two points of the ventricle led off, there will follow on each excitation a rapid electrical variation (lasting only a few $\frac{1}{100}$ sec.), in the direction of a current from the

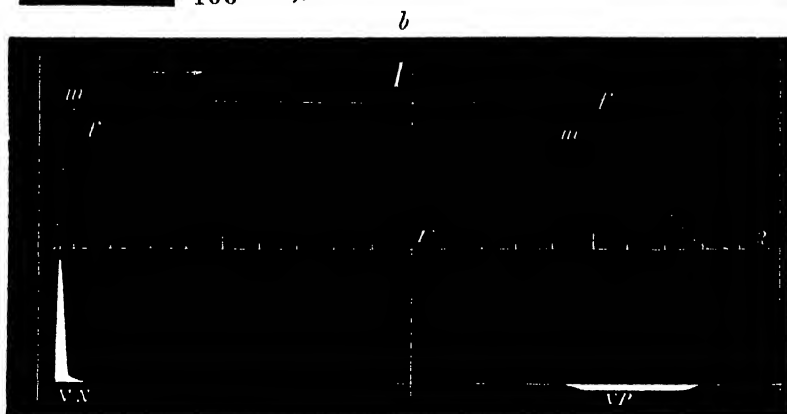


FIG. 127. —*a*, *b*, Diagrammatic representation of the electrical variation in an artificial cardiac contraction (Burdon-Sanderson and Page). The continuous line corresponds to the process of negativity at the electrode nearest the seat of excitation. The dotted curve, on the contrary, gives the negativity at the more remote contact. The middle line marks the time in $\frac{1}{100}$ sec. (*VN*) corresponds with the negative, (*VP*) with the positive variation on Bernstein's rheotome.

seat of excitation, succeeded by a longer period (1 — 2''), during which no current is indicated by the galvanometer; this is followed by an opposite phase of deflection (positive variation) which is much weaker and more prolonged than the initial "negative" variation. The interval separating the two phases corresponds exactly with the duration of the ventricular contraction, so that the one (negative) phase of the action current marks the beginning, the other (positive) the end of the excitation (contraction) of the muscle. The first phase of the action current obviously corresponds with the very short period during

which the wave of negativity is already at the leading-off contact nearest the seat of excitation, but has not yet reached the more remote contact. The subsequent stage of no current (and apparent rest) corresponds with the period during which both points led off are at the maximum of negativity (excitation). The positive phase at the end corresponds with the moment at which negativity is already diminishing at the leading-off contact next the seat of excitation, but still obtains unimpaired at the further contact.

Fig. 127, *b*, is a graphic record of the time-relations of the excitatory wave in the ventricle of the frog's heart. Easy as it

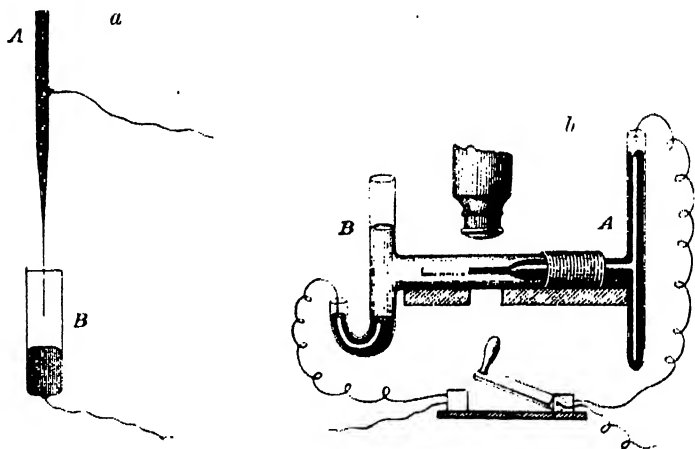


FIG. 128.—*b*, Capillary electrometer. (Fredericq.)

is with the modern, sensitive galvanometer to demonstrate the P.D. due to spontaneous, or artificially induced, rhythmical activity of the heart, another method that has been much used of late, is still more advantageous; this is the *capillary electrometer*. This instrument, invented long ago by Lippman, but first used by physiologists at a much later period, consists essentially of a glass tube, drawn out into a fine capillary (Fig. 128, *a* and *b*, *A*), the open end of which dips into a vessel (*B*) filled with dilute sulphuric acid. The behaviour of the meniscus in the capillary tube is observed with the microscope. If current enters the capillary in one or the other direction, the surface polarisation will produce a change in the constant of capillarity, with a

corresponding displacement of the mercury meniscus. The quicksilver in the capillary responds even to excessively rapid variations of the current; but the instrument seems more especially appropriate to experiments on the cardiac action current.

Marey (37) was the first to use this instrument in determining the electrical phenomena concomitant with the cardiac systole. He found that on leading off from the ventricle of the frog or any other animal, the electrometer gave a single oscillation at each systole. If the entire heart is connected with it, two oscillations can be observed in the column of mercury. The one is referred by Marey to the auricular, the other to the ventri-

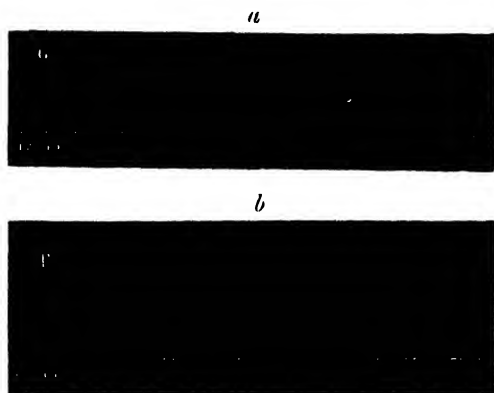
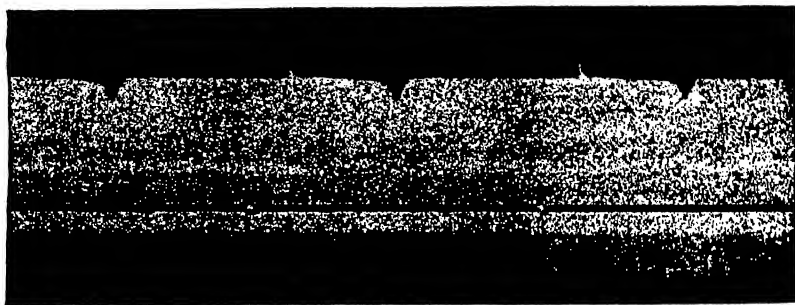


FIG. 129.—Photographic record of cardiac action current. *a*, In the Frog's heart; *b*, in the heart of Tortoise. Time-marking in seconds. (Marey.)

cular systole. Marey also succeeded in fixing these movements by photographing the image of the mercury meniscus upon a very sensitive plate moving at uniform speed. He concluded from these experiments that there is at each systole only a *simple* variation of current (Fig. 129, *a* and *b*). Burdon-Sanderson and Page employed this method as a means of controlling and completing their rheotome experiments. There appears to be a fundamental coincidence between the "theoretical" curve (constructed from rheotome experiments) of the variations in the frog's heart excited at one point of the ventricle, and that projected on to sensitive paper by the mercury column of the capillary electrometer. This appears directly from comparison of the two Figs. 172, *b*, and 130, *a*. It may be seen on the

photogram that the first "phasic action current" follows the excitation at a short interval, the apex being for an infinitesimal period, and very rapidly, positive to the base of the ventricle, after which there is a longer interval, in which the electrometer shows no deflection; then follows immediately the somewhat longer second (positive) phase of the action current, when the apex is negative to the base. On injuring the ventricle at one

a



b



FIG. 130. — *a*, Photographic record of action current in the Frog's heart, with artificial excitation (as in Fig. 127, *a*). The interruptions of the dark line mark the moments of excitation. *b*, Photographic record of action current after injuring the apex of the ventricle. The variation becomes monophasic. (Burton-Sanderson and Page.)

of the two leading-off contacts, one phase of course disappears, and the variation becomes purely negative, *i.e.* monophasic (Fig. 130, *b*). Similar tracings of the spontaneously beating heart have been photographed by other investigators, *e.g.* Fig. 131, A. D. Waller,—which at first sight differs from the results of Sanderson and Page, but coincides essentially with them. Here we have a simultaneous record of the contraction curve (*h, h*), and the effect (*c, c*) produced on the capillary electrometer by the

current of action in the spontaneously beating frog's ventricle. As may be seen, the first phase of the action current begins perceptibly earlier than the contraction; the negativity of the former (depression of the meniscus), corresponding with the maximum P.J. between base and apex, is reached long before the maximum of contraction, upon which a reversed current ensues as the second phase, when apex becomes negative to base. In Fig. 131, (t) is the time in $\frac{1}{20}$ sec. The capillary electrometer is so connected with the base and apex of the ventricle, that the effect is downwards, when base is negative to apex.

Cardiac response in the tortoise, and, as shown by A. D. Waller and Reid (39), in warm-blooded (mammalian) animals, is



FIG. 131.--Curve of contraction (h) and action current (e) of spontaneously beating Frog's heart. (A. D. Waller.)

also analogous with that of the frog. With artificial excitation of the excised and already quiescent ventricle, the proximal electrode is found to be at first negative, and immediately after positive, to the distal electrode, and a diphasic variation is thus produced, in consequence of the two phasic action currents, similar in all respects to that of the frog's heart. Owing, however, to the much greater velocity of excitation in the heart of warm-blooded animals, and the abbreviated period of contraction, the two phases merge into each other, as in striated skeletal muscle. Fig. 132, which is a photogram of the movements of the capillary electrometer with a normally beating and artificially excited mammalian heart, shows plainly that each phase corresponds with a *simple* variation, in the sense of a single excitatory wave. The capillary electrometer also shows a normal

diphasic variation, during spontaneous activity of the mammalian heart, when led off from two points of the ventricle (base and apex). But while in this case the *base is at first always negative* in the frog's heart, corresponding with the invariable direction of the excitatory, or contraction, wave from base to apex—in the mammalian heart (although this is generally the case, as appears from the recent experiments of Bayliss and Starling, 40) there are obvious exceptions, in which, by reversal, either the apex becomes negative earlier than the base (which Waller, *l.c.*, holds to be normal), or there is only a monophasic variation. In this last case there has usually been some injury to one of the points led off, by lesion, etc. Bayliss and Starling (*l.c.*) find that it is possible by unequal warming, or cooling, of the ventricle in the spontaneously beating dog's heart, to reverse the direction of the two phasic action currents. It is even sufficient to warm or cool the inspired air.

By means of the capillary electrometer it is possible to show the phasic action current of the heart in the uninjured body of an animal, or man, either by pushing two fine needle electrodes through the breast-wall into the ventricle, and connecting these with the electrometer, or by leading off from different points of the body-surface (41). In this case a lead-off from the mouth is equivalent to leading off from the base of the ventricle—a lead-off from the rectum, or from a posterior extremity, to leading off from the apex. In addition, the following combinations were found (on man) to be favourable for leading-off (cf. Figs. 133 and 134):—

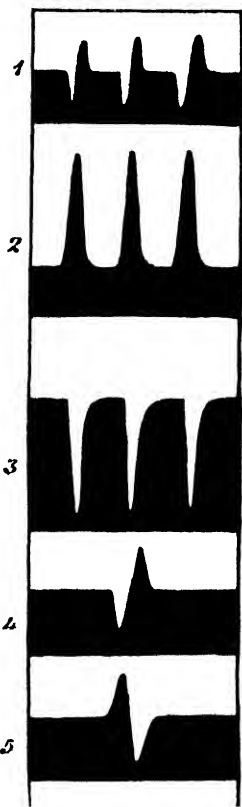


FIG. 132. Photographic record of action current in mammalian heart, investigated with the capillary electrometer. 1. Spontaneous beat of the heart; the first phase corresponds to negativity of apex to base, the second to the reverse action. 2. After injury to apex of ventricle. 3. After injury to base of ventricle. 4. Excitation effects with artificial excitation of apex. 5. Excitation effects with artificial excitation of base. (A. D. Waller.)

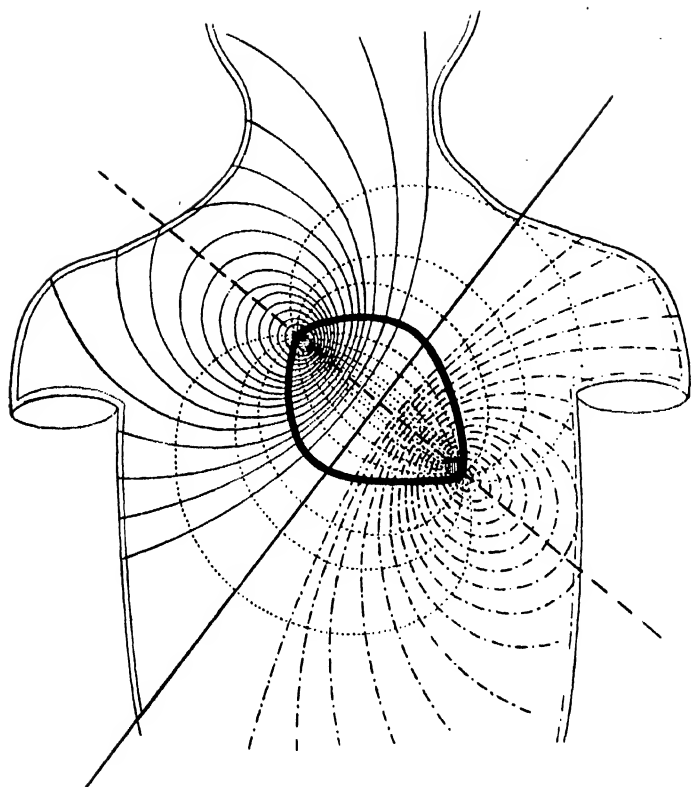


FIG. 133.—Schema of the distribution of potential (lines of current diffusion) arising from the action current in the human heart. (A. D. Waller.)

ELECTROMOTIVE ACTION IN MUSCLE

Left hand and right hand.
Right hand and left foot.
Mouth and left hand.
Mouth and right foot.
Mouth and left foot.

} Fig. 134.

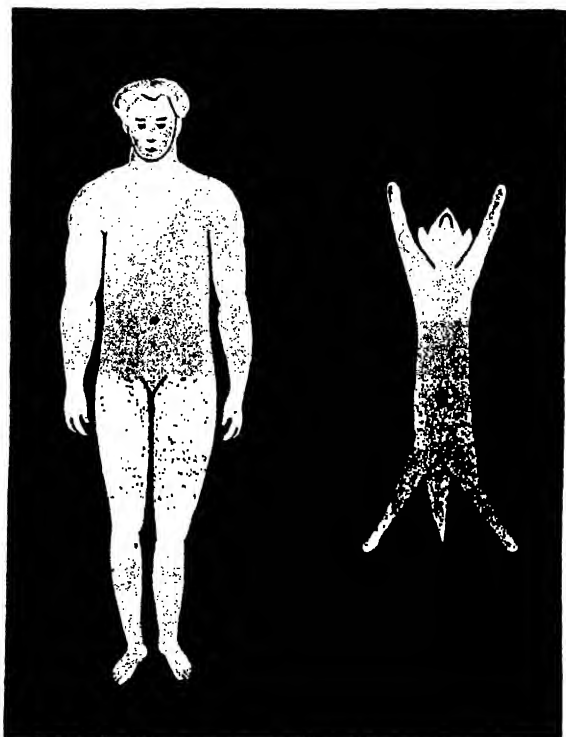


Fig. 134.—Schema of distribution of potential caused by the cardiac action current at the body-surface in Man, and in the Cat. The dark parts correspond with the lead-off from the apex, the lighter with the lead-off from the base. (A. D. Waller.)

The unfavourable combinations were :

Left hand and left foot.
Left hand and right foot.
Right foot and left hand.
Mouth and right hand.

These facts may be explained by the distribution of the lines of current, or potential, in the body (corresponding with the action currents of the heart). In mammals the approximately median

position of the heart obviates this striking asymmetry in the distribution of differences of potential, which is due to the activity of the cardiac muscle. These experiments also yield di- or even triphasic effects (Fig. 135), and according to Waller's earlier observations, the apex of the heart is invariably negative at first, corresponding with a basal direction of the wave of excitation.

Owing to the extraordinary sensitivity of the capillary electrometer, and its very rapid reaction, it gives us a direct reading of the action current of striated skeletal muscle, when tetanised. If the capillary electrometer is connected with the secondary coil of an induction apparatus, each interruption or closure of the primary circuit produces a visible movement of the meniscus in the capillary (with a proper adjustment of the coil).



FIG. 135.—Simultaneous record of cardiacum (*h*) and skeletal musculum (*e*). (C. A. W.) Waller

With Neef's vibrating hammer, the single oscillations fuse into a gray margin, which with reduced strength of current seems to blot out the sharp image of the mercury meniscus, and with increased current rises above it in measurable proportions. On applying a battery current with correspondingly rapid interruptions, and uniform direction, the meniscus exhibits a total shifting in the direction of the current. This, like the oscillations, is smaller in proportion as the number of interruptions is greater, and *vice versa*. In order to detect the gray margin at high frequency, along with the total shifting, greater strength of current is required than at a lower frequency of interruption (Martius, 42). This is important in judging the observations made with the instrument, since a physiological process accompanied by electromotive action can record itself on the capillary

electrometer by a total shifting only, *without oscillations*, although unequal variations of current are present which fail to appear in the meniscus, because the oscillation frequency is either too high for the existing E.M.F., or too low in proportion with the electromotive frequency. There are two ways of recording the rapid oscillations of the meniscus; the beats may be photographed on a rapidly-moving sensitive plate, which is not difficult with the present development of instantaneous photography (unfortunately no methodical investigation of the action currents in skeletal muscle has yet been undertaken in this manner): or the form and time-relations of the movements of the meniscus may be read off directly by the stroboscopic method. Martius (*l.c.* p. 590 ff.) attached a paper flag, 1 cm. square, instead of a writing-point, to the lever end of a very sensitive electro-magnetic Pfeil's chronograph. If this instrument is introduced into the circuit of the interrupter, the lever will swing in the period of the interrupting spring. The paper flag, at a sufficient frequency, exhibits a broad, gray margin at its upper and lower edges, while the flag itself appears quiescent. If the oscillating meniscus of the capillary electrometer is observed through the lower or upper margin, its oscillations vanish altogether, and it appears sharp and fixed *if it and the flag are vibrating at the same period*. Now since both oscillations are produced by the same interrupter, it is obvious that the mercury has no intrinsic vibration period, but exactly repeats the oscillations of the interrupter; seeing that every frequency of the latter (up to 100 per sec.) obliterates the vibrations, *i.e.* gray film, of the meniscus, as previously visible in the stroboscope. It is clearly easy with this method to determine objectively the unknown frequency of periodic variations of current, read off in the oscillations of the meniscus, if two interrupters are used, one of which is connected with the capillary electrometer, the other with the stroboscope in a separate circuit. If the vibration period coincides in the two interrupters, the oscillations of the meniscus are neutralised. If they differ, interferences arise, from which it is easy to calculate the amplitude of difference in vibration in the two springs (Martius, *l.c.* p. 591). Let the rate of vibration in the stroboscope be 18 per sec. If, instead of frequent oscillations of the meniscus (which can only be counted artificially), two regular beats are observed

per second through the margin of the stroboscope, it follows that the interrupting springs differ by two beats. Martius tested the physiological applicability of the method (*L.c.* 592) by leading off from longitudinal and transverse section of the frog's gastrocnemius to the capillary electrometer by unpolarisable electrodes, the current of rest being compensated. On exciting the sciatic by 18 break induction shocks per sec. the meniscus exhibited regular and visible oscillations; the stroboscope was then introduced into the primary circuit of the induction apparatus, so that the flag vibrated synchronously with the number of stimuli, when the oscillations of the meniscus were extinguished—thus proving that a negative variation corresponds with each impact of stimulation in the muscle, an oscillation of the capillary meniscus with each negative variation. The same effect is produced with a stimulation frequency of 30 per sec. Unfortunately, we have thus far no systematic analysis of strychnin tetanus, spasm in electrical excitation of the spinal cord, or the voluntary and reflex movements of the frog, by this method. Lovén's analysis (43) of voluntary muscular contraction in the frog and crab with the capillary electrometer yielded interesting results, and has recently been confirmed by v. Kries.

Lovén convinced himself that the persistent voluntary contraction of the crab's muscles, as well as strychnia spasms in this animal and the frog, are accompanied by definite and fairly regular variations of current. The frequency of these was astonishingly low (about 8 per sec.) That such infrequent twitches should fuse into a persistent contraction is the more remarkable, since we know that 20 or more excitations per sec. are required to produce complete tetanus on the frog with electrical excitation, and according to v. Limbeck's observations 34 stimuli sent into the spinal cord can be transmitted to the muscle. Lovén finds himself reduced to the hypothesis that single voluntary twitches travel more slowly than those provoked by electrical excitation. These results tally with those of Del-saux (44) (Fig. 136, *a* and *b*), who only observed five oscillations per sec. with the frog's gastrocnemius in strychnia tetanus, on the capillary electrometer. The simultaneous record of change of form and electrical variation in muscle showed complete coincidence.

Since the telephone, like the capillary electrometer, is ex-

cessively sensitive to a brief duration of current (variations of current), it was natural to apply it to the determination of the current of action in muscle. Hermann (45) was the first to experiment with the telephone, but he failed to detect any action current. Bernstein and Schoenlein (46), on the other hand, obtained positive results in 1881 with Siemens' telephone. If 4 to 6 frogs' gastrocnemii were laid in working order upon non-polarisable electrodes (pads), and their nerves simultaneously excited, a "crackling sound" was plainly audible in the telephone, which diminished in clearness with prolonged excitation. Further

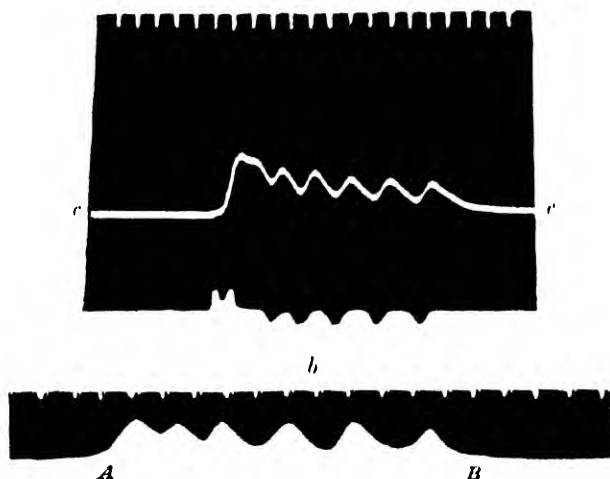


FIG. 136. —Photographic record of action current in Frog's gastrocnemius in strychnine tetanus (c, c'), curves of contraction. (Delaux.)

investigations were carried out on the rabbit. The gastrocnemius muscles were exposed and connected with the telephone by unpolarisable electrodes, or simple metal needles were pushed through the skin into the muscle, and thence led off to the telephone (Bernstein, 47). In both cases audible tones were obtained, provided the sciatic nerve, which had previously been divided, was tetanised. It was found, on exciting with the acoustic current interrupter, that the number of stimuli might reach 700 per sec., when the note in the telephone, corresponding with the interrupter, was heard with musical integrity. Every note sung into a second telephone (exciting telephone to sciatic) was clearly distinguish-

able from the muscle telephone, and had its own characteristic pitch. After poisoning with strychnia also, a deep singing tone was clearly audible in the telephone at the commencement of a spasm. Later on, Wedenski (48) succeeded in hearing the action current of a single gastrocnemius in the frog, with intact circulation, led off by two needles, in the telephone, both with artificial electrical tetanus, and during voluntary contraction, and chemical excitation of the nerve.

Hesselbach, who worked under Bernstein's directions, pointed out that even a simple twitch from a single induction shock produced an audible sound in the telephone; which is important with regard to the origin of the first cardiac bruit, and the nature of systolic contraction. To exclude reflexes and voluntary movement, the sciatic of the rabbit's thigh was divided; single induction shocks were then led in by two needle electrodes pushed into the gastrocnemius muscle. A momentary dull sound was then quite audible in the stethoscope at every twitch, and also when all change of form and alteration of position in the muscle were excluded by enclosing the ends in plaster of Paris. The "*electrical sound*" produced by the concomitant variation of current must be distinguished from the "*mechanical sound*" that is heard directly by the ear in the muscle; according to Bernstein, however, the two sounds coincide in time. Bernstein concludes that in listening to the bruit, or tone, of the muscle, we do not hear the process of the twitch, or contraction, but that molecular process which is electrically expressed in the action currents; this, however, postulates that the electrical variation *as a whole* precedes contraction, which we have seen reason to doubt in the previous discussion.

We remarked above that every contracted muscle must be regarded as in a state of excitation, while it by no means follows that excitation is always accompanied by corresponding change of form. From this point of view, therefore, it seems not impossible that electrical effects may arise, under certain conditions, without concomitant phenomena of contraction. It has long been known that this is the case where there is a passive block in the muscular contraction, and Fano and Fayod (49) showed that in the auricle even rigid tension did not prevent the development of rhythmical action currents, nor are they quelled during the systolic stand-still after poisoning with digi-

talis. We may also refer to the observations of Kühne (50) on muscles treated with NH_3 vapour, and strongly contracted, which still exhibited very striking secondary effects, when all trace of movement had been abolished. This occurred on making a new section, which implies that there may still be effective waves of excitation in the muscle without any subsequent contraction wave. Similar experiments on the adductor muscle of the crab's claw (Biedermann) will be referred to below.

Fano and Fayod made the important observation that the "electrical pulse" of the auricle in the tortoise heart may even increase when immobilised by tension; this recalls the striking effect of tension on all muscular processes, in regard no less to mechanical yield of work than to thermic relations. In this connection, too, is the beneficial effect of tension in normal striated muscle upon secondary activity (51). Meissner and Cohn observed that with indirect excitation of the muscle the secondary (exciting) effect increased when the primary muscle was tetanised during tension. Even in single twitches this is easily demonstrated on muscles in which the excitability has perceptibly diminished. The latter is a *sine qua non*, because experience shows that with high excitability of the primary preparation, the secondary twitch will reach its maximum with even low excitation. At a certain stage of exhaustion, *e.g.* after long heating, it is found that the capacity of giving secondary contractions when unloaded is entirely lost by the muscle (gastrocnemius of *R. temporaria*), although even a weak excitation from the nerve will produce strong primary contractions. Even with strong excitation, and highly sensitive secondary preparations, the latter are not affected. In every case the secondary efficiency of the primary heated muscle is restored immediately after loading, or any kind of tension, to disappear again as soon as the strain is removed. Up to a certain limit, the magnitude of the secondary twitch increases with the load, but soon becomes maximal, and it cannot be *prima facie* determined whether the factors which produce such a marked augmentation of secondary activity during extension increase it still further with constant increase of loading. In the parallel-fibred sartorius also this effect of tension may be elegantly demonstrated. Since we cannot doubt that the secondary action of a muscle upon the superposed nerve of another preparation is induced solely by

the wave of electrical variation set up in the latter, directly, or by excitation from the nerve, there can only be two alternatives as regards positive change of sign in secondary action; either the conditions for neutralisation of the existing P.D. by the supposed nerve become more favourable, or the magnitude, form, and velocity of the wave alter in a direction more favourable to excitation of the former. That the first of these possibilities does not come into the present consideration may be concluded from the fact that the experiment comes off as well with regularly constructed muscles as with the usual nerve-muscle preparation. Moreover it is possible, by altering the position of the secondary nerve on the surface of the primary muscle, to render the external conditions of the discharge of secondary twitches during extension as unfavourable as possible, either by only allowing it to come into contact with a very short strip of the extended muscle, or by placing it across, or round, the muscle, which, however, in the majority of cases has no effect on the result. Only the other possibility, therefore, need be considered, and the magnitude, form, and velocity of the wave of electrical variation have therefore been investigated comparatively in stretched and unstretched muscle. Heidenhain, *e.g.*, was the first to show that the proportion of vital energy developed as heat in contraction depends essentially upon muscular tension, since, up to a certain point, the evolution of heat increases with the loading. This suggests the idea that the other factor in the sum of energy, which appears as electricity in the action current concomitant with excitation, may be influenced in the same degree by tension. The experiments of Lamansky (*Pflügers Arch.* iii. p. 193), who observed an increase of the negative variation in the gastrocnemius with increase of loading, would be in favour of this assumption if the exclusive use of the irregularly constructed gastrocnemius did not suggest objections already pointed out by du Bois-Reymond.

If this theory is correct it might be expected that other data, which are experimentally found to augment the capacity of work in the muscle, would also increase its secondary activity. The favourable influence exerted under some conditions by *repeated* excitation, at uniform intensity, upon the mechanical capacity for work in cardiac and skeletal muscle, where a "staircase" is formed at the beginning of a series of contractions, has already been referred to.

Electromotive action does therefore, under the same conditions, seem at times to undergo a considerable augmentation. If properly excitable gastrocnemii of "cold frogs" are employed as primary preparations, a more or less crowded series of twitches appears—independent of loading or not loading—with slow rhythmical excitation by the make and break of a primary induction coil, each of which is also followed by a *secondary contraction*, so that the beginning of the primary series coincides with that of the secondary series of twitches. And, in conclusion, if primary twitches are summated into a steady, uniform tetanus by accelerated excitation, this is no less the case as a rule with secondary preparations. The primary sets up a secondary coincident tetanus. The effect is quite different when a warm-blooded muscle is used as the primary preparation, for, when it is unstretched, even the strongest excitation fails to produce secondary twitches. Thus—apart from the temporary state of excitability of the preparation—it depends solely upon the length of the interval which separates the single stimuli, whether or no the secondary inactivity of the muscle continues during the whole period of incomplete tetanisation.

As a rule, when the test-nerve is placed upon the surface of the primary muscle, the latter excites the secondary preparation after a longer or shorter series of ineffective twitches. The secondary twitches are small at first, but rapidly increase in magnitude, and may finally far out-top those of the primary preparation.

Since the contractions of a warm-blooded muscle become more extended at a certain stage of fatigue, at which, more particularly, elongation takes up a longer period, it may happen that with even a moderately rapid succession of single stimuli, the twitches of the unloaded, primary preparation fuse into almost constant tetanus, the vigorous and perfectly distinct secondary twitches alone expressing the internal changes of the muscle, which correspond with each stimulation-impact; the same occurs also in tensely stretched muscle. It has already been stated that the period for which the unstretched gastrocnemius muscles exhibit secondary activity during incomplete tetanus, is conditioned on the one hand by the degree in which the specific muscular state induced by heat is developed, and on the other by the intensity and number of the successive stimuli in the time-unit. Here we need only say that the delay seems generally to

be greater, in proportion as the induction current is weaker, and the excitation intervals, with a given state of excitability, longer. Often the secondary muscle only begins to twitch when the stimulation of the primary muscle has already lasted some minutes, and when, owing to fatigue, the changes of form in the latter, corresponding with the single stimuli, are hardly to be recognised. It is natural to suppose that this might be solely an effect of summation in the secondary nerve, but that is easily excluded by applying the nerve, not at the beginning of excitation in the primary muscle, but after a greater or lesser number of stimuli. Without exception the secondary twitches appear in full vigour as soon as the nerve is brought into contact with the primary muscle, showing that the gradual development of activity in the latter depends upon changes in its substance produced by repeated excitation.

If in these two cases it appears highly probable that the difference in the secondary action from muscle to nerve depends upon the intensity of electrical action in the former, in other instances disparity of time-relations, and form, of the wave of electrical variation, seem to be the determining factors. Above all there is the striking difference in secondary action from muscle to nerve, when the former is *directly* excited in a variety of ways. As a general rule it is harder to elicit secondary contractions when the primary muscle is excited directly, than when it is excited from the nerve. Du Bois-Reymond in fact supposed that there was no secondary twitch, if a wave of excitation was set up in the sartorius or gracilis, with a sciatic nerve lying on the excitable upper end of the muscle. Kühne was the first to show, on the contrary, that the twitch produced by moistening the fresh section of a curarised sartorius with a conducting fluid (which Hering proved to be electrical in character) is peculiarly adapted to secondary action, a fact which only makes it more remarkable that the direct electrical excitation of the same muscle by artificial currents should be so ineffective for this purpose. Kühne did, indeed, observe unmistakable secondary action on exciting one end of a muscle with single induction shocks, but in all these cases such a strong current was needed that special control experiments were required to exclude direct excitation of the secondary nerve by current diffusion. If a battery current is thrown in laterally by unpolarisable electrodes near one or

the other end of the frog's sartorius, connected at both ends with the bones, the strongest excitation fails to produce any trace of secondary action,—notwithstanding a marked twitch of the primary muscle and favourable position of the test-nerve,—so long as both (thread) electrodes are placed on the continuity of the muscle, so that the lines of current must traverse it in a more or less oblique direction at the point where they enter, as well as leave, the muscle. No alteration of this negative result can be detected, however much the muscle is extended. On the other hand, secondary effects of great intensity may regularly be seen with weak excitation of the primary muscle, if the galvanic current leaves the muscle, at either end, by the natural uninjured ends of fibres (51). It is sufficient to connect up one electrode (kathode) with the stumps of bone, and to place the other, by which the current enters, directly on the muscle. The secondary twitch occurs with *one* direction of current only, while closure in the other direction is followed by a vigorous twitch of the primary muscle, without excitation of the second preparation. It is not improbable that with simultaneous and equal excitation of the collective ends of fibres on one side of the sartorius (as occurs when the current leaves the muscle by one or the other end in the longitudinal direction of the fibres), the wave of electrical variation might be essentially distinguished from that which is discharged with a more or less oblique exit of current through an electrode placed at the side of the muscle. In every case, however, we must assume that the excitatory wave discharged by immersion of a fresh transverse section in conducting fluid, owes its peculiar aptness for secondary action to the same condition as the wave produced by closure of an atterminal battery current, so that the secondary inefficiency of the directly excited curarised muscle is only apparent, and produced by purely external conditions.

With regard to these experimental results, it is very striking that the position of the secondary nerve on the primary muscle should have comparatively little influence on the consequences. If, as it is impossible to doubt, this is an electrical excitation of nerve by the action current of the primary muscle, two points must be connected which present a considerable difference of potential at a given moment. The most favourable position of the secondary nerve is apparently that in which it lies upon the

lower surface of the sartorius, parallel with the fibres of the muscle, and as much extended as possible. Then, under some conditions, the thinnest bundle of muscle-fibres, hardly corresponding in diameter with a frog's sciatic, will suffice, on exciting the transverse section, to produce secondary contraction. For the rest, with moderate excitability of nerve, hardly any position fails to produce vigorous secondary contraction of the muscle. Secondary excitation in which the nerve bridges the muscle at right angles, has a special interest. This is easily effected if the sciatic of the leg, fixed on a movable glass plate, is clamped, along with the sacral plexus, to a conveniently fixed glass rod, and applied, after moderate extension, to the inner surface of the dependent sartorius, or simply hung over it. In the latter case the most vigorous secondary contraction is found on making a double transverse section in the sartorius with both ends pendent, or by moistening it in the usual way (Kühne, 5); it then appears that the secondary activity of this most regular muscle, on which du Bois' law of the muscle current can be infallibly demonstrated, is independent of the amplitude of the current of rest to such a degree that there are actually no points or lines on the muscle excited from the cross-section which fail to give secondary action. Even more surprising than secondary excitation with the nerve laid across the primary muscle, is the fact that application to the surface of the transverse section of the muscle does not abolish secondary action, which does not harmonise with the prevailing view of the dependence of secondary excitation upon the muscle current (Kühne, *l.c.* p. 24 f.); under these conditions, indeed, it might almost be doubted if the wave of electrical variation is really the immediate cause of secondary excitation. Kühne (*l.c.* pp. 27-37), however, gave a direct proof that it is so, by showing that the part in contact with the secondary nerve did not act at the same moment as that in which the primary excitation impinged on the muscle at another and more remote spot, but as much later as was required by the wave of variation to pass from its point of origin to that at which it is led off. The nerves of two gastrocnemii were laid on the sartorius at some distance from each other, and the muscle was then excited from one end. The interval between the excitations of the two secondary nerves was always quite evident, and often considerable, although excessively fluctuating. While in the

most unfavourable cases the process excitatory of secondary contraction is propagated at a velocity of 25 cm. per sec., *i.e.* very slowly, the velocity in other cases is so great that the methods employed (by which velocities at 2 m. per sec. can be estimated) were unable to determine it. It appeared even from Bernstein's first experiment that the velocity of the wave of electrical variation in muscle is extremely fluctuating, and diminishes with comparative rapidity in the excised muscle. If the period of the *contraction wave* is any guide to that of the wave of variation, we might recall the well-known waves of contraction, visible to the eye on account of their slowness, which appear more particularly in insect muscle, but also under some conditions in the freshest frog's muscle, *e.g.*, as above, in the sartorius or adductor magnus, when mechanically excited with the point of a needle (Kühne, *l.c.* p. 36 f.), or as the galvanic wave, with strong battery currents.

With regard to the question, which section of the electrical wave of variation is most important in secondary excitation, we should *a priori* be disposed to choose the foremost, *i.e.* the steepest, as most efficient. In any case it is—as follows from the evidence given above—a very *short* segment of the excitatory wave which excites the nerve resting upon it.

In all effective nerve-excitation (more particularly electrical) a certain rapidity of time distribution is implied in the changes set up by the stimulus; and this appears in secondary excitation from muscle to nerve also, since sluggishly-moving muscles are for the most part unfitted to produce secondary excitation in frog's nerve.

Matteucci stated that the secondary contraction failed when he applied the frog's sciatic nerve to the excited muscular mass of the intestine, stomach, or bladder. Kühne confirmed the same in the highly mobile ureter of the rabbit; nor could he discover secondary action in the striated muscles of *Hydrophilus* and *Astacus*, even when, in the latter, the primary contraction of the adductor claw-muscle was produced by excitation of the nerve. So again the intestine of the tench, which, at the part where there are striated muscles, contracts tolerably rapidly, and almost twitches, with electrical excitation. Kühne also found total absence of secondary action in the muscles of *Emys europæa*, both in the pale muscoli retrahentes capitis collique and the red

muscles of the limbs, on applying electrical excitation to the former directly (by puncturing the spinal cord, or excising one end), to the latter from the nerve-trunk. Since the tortoise can withdraw its head with tolerable rapidity, and almost twitches its legs, at least when its nerves are artificially excited by induction shocks, its failure of secondary response both to single twitches and to tetanus is very remarkable. The extent to which secondary excitation from muscle to nerve (frog) is dependent on the velocity of the excitation (contraction) wave is elegantly shown in the heart. While Kühne (*l.c.*) obtained only weak secondary twitches from the ventricle of the beating tortoise heart, which disappeared soon after exciting it, *i.e.* long before any perceptible diminution of pulse, the smaller but more rapidly beating frog's heart responds much better, and the still more rapidly pulsating mammalian heart notably gives vigorous secondary contractions. On the other hand, Kühne obtained, on exciting the nerve, as good secondary twitches and secondary tetanus from the red gastrocnemius, as from the pale muscles of the rabbit, although its twitch is essentially more sluggish.

J. v. Uexküll (52) found that with uniform conditions, an important factor in the results of secondary excitation was the point at which the primary muscle (non-curarised sartorius) was excited. "The simultaneous excitation of muscle-substance and nerve transversely to the entrance of the latter into the sartorius produces no secondary reaction, while pure muscular excitation, like pure nerve excitation, results in secondary action under the same conditions." Uexküll showed by experiments on the gracilis muscle that the occurrence of secondary effects is associated with the coexcitation of the nerve-endings. Under certain presumptions (*i.e.* a latent period for the propagation of excitation from the nerve end-organ to the muscle, and secondary activity of the *summit* only of the variation curve of the action current) the phenomenon might be explained as one of interference. Uexküll formulates the process as follows: "A stimulus reaches the nerve end-organ and muscle-fibre simultaneously, it discharges a wave of action in the latter which would throw the secondary limb into excitation, were it not that the simultaneously excited end-organ of the nerve discharged itself a moment later upon the muscle. Hence instead of a simple action wave there are two waves coupled together. These waves are inept for secondary

action, because they are flattened. The whole process, therefore, loses in crispness, and also in capacity for exciting."

These conclusions leave no doubt as to the influence which the intensity, form, and distribution in time, of the electrical wave of variation exert upon the secondary excitation of nerve and muscle. It remains to consider the effect of the time-order of successive (single) stimuli upon secondary excitation and upon electrical response of muscle in general.

Since secondary excitation is only a special form of the electrical stimulation of a nerve still in connection with its muscle, we should *a priori* presume that the same law which dominates the manifestation of primary tetanus, and more especially its dependence on the intensity and frequency of stimuli, also holds good for secondary tetanus. Remembering further that the electrical waves of variation are not always exactly parallel with the phenomena of contraction, we should not expect complete parallelism between primary and secondary tetanus (as actually appears from the facts). Before the incapacity of many tetani to produce secondary tetanus was appreciated, the latter was held to be such an unfailing indication of primary tetanus that it was appealed to, not merely in evidence of the electromotive discontinuity of all tetani, but also in deciding between contracture and tetanus. It was taken for granted that a muscular movement which induces secondary twitch, but not secondary tetanus, must itself be a simple twitch. Yet this often occurs where there is no doubt as to the discontinuity of the primary stimulus. The effect in the secondary preparation depends essentially, as can readily be demonstrated, on the character and strength of the primary excitation, and therefore on the intensity and frequency of the induction shocks sent into the primary preparation. If the strength of current is so adjusted that the primary muscle is thrown into tetanus, there will be a partial tetanus in the secondary muscle varying in length and height, or curves will be yielded which cannot in any way be distinguished from those sometimes described by the primary muscle as "initial twitches." In rare cases we find not merely a secondary initial twitch at the beginning of primary tetanus, but also a secondary "final twitch" at the end of the excitation (Schoenlein, 53). If the secondary initial twitch appears at relatively low stimulation-frequency, it is mainly due to those

changes in intensity and duration of the action current in the primary muscle, which must be regarded as fatigue effects, as is attested by the reappearance of secondary tetanus, when the primary muscle has had a certain time to recuperate. Thus Morat and Toussaint (54) observed secondary initial twitches, with fatigue of the primary muscle, at a frequency of 70–80 stimuli per sec. Where fatigue is as much as possible eliminated, secondary tetanus may be kept up by strengthening the primary excitation, within a wide range of frequency.

While the primary tetanus discharged by rhythmical excitation, electrical or mechanical, does for the most part elicit secondary tetanus also (though not always coextensive in duration), in other forms of artificial tetanus this never is the case; although in favourable examples secondary twitches may be elicited. As we shall see later, striated skeletal muscle falls, under certain conditions, into prolonged tetanus while the nerve is traversed by a constant current (closure tetanus), and occasionally after the opening of the circuit also (Ritter's opening tetanus). J. J. Friedrich (55) found that the secondary preparation in such a case responded only, if at all, by a secondary twitch at the commencement of the tetanus under observation, never by a secondary tetanus. It is, moreover, remarkable that the effect was much more often absent in opening, than in closure, tetanus.

The tetanus induced by *chemical* excitation of motor nerves, though often pronounced, is equally inefficient as regards secondary tetanus (Kühne, *l.c.* p. 61 f.) Salt tetanus and glycerin tetanus produce, as Kühne says, such a large mechanical yield of work from the muscle, that the failure of secondary tetanus cannot certainly be ascribed to weakness of muscular excitation; it must rather be owing to the local mode of attack of the chemical stimulus, or to its temporal relations, that the muscle responding indirectly to it exhibits such a different reaction.

This is the more remarkable since every mode of vital tetanus yields at most one or more secondary initial twitches, or intermittent secondary intermediate twitches, never secondary tetanus. Du Bois-Reymond investigated the question "whether strychnia tetanus, like electrical tetanus, is of an interrupted character": he arranged his experiment so that the test-nerve was applied to the natural longitudinal, and natural or artificial transverse

section of the leg muscles of a strychninised frog. In favourable cases, "the rheoscopic leg set up a series of weak twitches which, though connected, were never very close together"; it usually remained quiescent.

Friedrich (*l.c.* p. 422) made the same experiment on frogs, rabbits, and guinea-pigs. Single twitches, which preceded the spasm of tetanus proper, generally caused secondary twitches. An even (strychnia) tetanus, on the contrary—even if there was not, as frequently, a total failure of action—produced secondary twitches at the commencement only, never secondary tetanus. Effects, corresponding with those observed by du Bois-Reymond, occur only when the primary preparation, instead of exhibiting a steady tetanus, goes into clonic spasm. In other respects strychnia tetanus has a marked action on the superposed nerve. Strong secondary initial twitches accompany almost every spasm of rigor in frogs that have been kept in very dilute solution of strychnia, until for hours, and even days, they will exhibit heightened reflexes; the nerve need only be in contact with the skin of the leg in the intact animal (Kühne, *l.c.* p. 60).

Sustained voluntary and reflex contraction is as little apt to excite secondary tetanus as strychnia spasm. Harless was the first who tried to obtain secondary action from the exposed gastrocnemius of an otherwise intact frog, during its natural movements. Even when sustained contraction had been induced in the muscle by painful excitation, Harless failed to discover secondary tetanus; there was at most a secondary twitch at the beginning of the contraction. Exactly the same occurred in the reflex movements. Another experiment of Harless' is interesting, where (in the frog) first the spinal cord and then the sciatic plexus, high up, were electrically excited. In the former case a secondary initial twitch only appeared, in the latter there was invariably secondary tetanus. In this connection we may quote the observations of Hering on the contraction of the diaphragm in tetanus, occurring in respiration; it is not possible to obtain secondary tetanus of a frog's leg, with applied nerve, from the contracted diaphragm, although the same preparation falls into secondary tetanus directly the phrenic nerve is tetanised by weak electrical excitation, and gives a tertiary twitch if the nerve of the diaphragm is divided high up and laid on the still beating heart, so that the diaphragm is brought into

rhythmical secondary contraction by the heart-beat. A simple method of obtaining a whole series of secondary twitches from ordinary skeletal muscle, reflexly excited, is that given by Kühne (*l.c.* p. 63): a lizard's tail, amputated and curled up, produces vigorous excitation in the nerve of a frog's leg brought into contact with it. Natural rapid contractions do accordingly possess considerable secondary efficiency.

The telephone, as a proof of the discontinuous electrical wave of variation in muscle in natural tetanus, presents great advantages over the rhcoscopic test. Bernstein and Schoenlein (56) heard "a deep, singing tone of unmistakable clearness" on the strychninised rabbit at the outset of spasm. Later on Wedenski (48) organised a whole series of experiments in this connection. At each energetic natural contraction of triceps femoris in the frog, he succeeded in hearing a perfectly distinct murmur (aspiration) in the telephone. The same effects, only more intense and persistent, were heard during spasms produced by destruction of the spinal cord. Wedenski also experimented on himself (by pushing two needles into his biceps brachii), as well as on toulus, dogs, and rabbits. The animals were either poisoned with strychnia, or tetanised from the cord. In all these experiments a hardly definable, but deep and regular murmur or aspiration, was heard, like the sound of a distant waterfall. If the arm is held out for a considerable time, the murmur becomes weaker, and eventually dies out (fatigue). The sound is deep, but its pitch indeterminable; the attempt to determine it synthetically by artificial measures gave negative results, since excitations of 8-20 beats per sec. yielded electrical tones of a perfectly different character from the murmur heard in the telephone in *voluntary* contraction.

However completely the telephone may attest the oscillatory nature of the electrical processes in voluntary, active muscle, it has the great defect of giving no determination of frequency of variation.

The cause of the failure of secondary tetanus in the above-cited instances has been the object of repeated investigation. Du Bois-Reymond (1) pointed out the relative instability of voluntary and strychnia tetanus. Supposing the contractions of the different groups of fibres in a muscle not to occur simultaneously, it is conceivable that the electrical variations, led off externally, might

produce mutual disturbance or neutralisation, so that the effect on the superposed secondary nerve would be abolished, which is not the case when with rhythmical, artificial excitation of the nerve the collective elements respond in the same phase with a uniform reaction. More recently Hering (55) and Brücke have formulated a similar theory, and the latter expresses the relation figuratively by contrasting the artificial excitation from the nerve as a "volley," with the irregular discharge or "platoon fire" from the central organ. The inefficacy of the primary tetanus produced by chemical excitation of the nerve, with regard to secondary action, may be explained in the same manner. "If we imagine the secondary action of the muscle to proceed, not from a single muscle-fibre, but always from groups of fibres, and that in every such group the waves of variation run parallel with each other in no definite order, we have the conditions which result in negation of the external effect, since the neutralisation of the differences in electrical potential, which are the sole cause of all secondary excitation, proceeds in the muscle from one fibre to the other, from each negative point of the one to the less negative, or positive, of the adjacent fibre" (Kühne, 50). Hence it only remains to find the *rationale* for the early expiration of secondary tetanus, or appearance of the secondary initial twitch, with the rhythmical "volley" of electrical, or mechanical, excitation. This presents no difficulty, provided the conditions of the appearance of the *primary* initial twitch, and more particularly its dependence on the intensity and frequency of the tetanising stimuli, are kept in mind. According to the capillary electrometer and telephone, the intensity of the electrical variations of the muscle declines very rapidly, and in each case much earlier than the contraction. If in addition to this the stimulation-frequency is considerable, we have sufficient ground for the brief duration of the secondary tetanus.

There is yet another factor to which Kühne (*l.c.* p. 68) first drew attention. A striated muscle notably presents no physiological entity, since at least two functionally distinct kinds of fibres enter into its composition. It only requires a different *tempo* in the rate of alterations of velocity in the dark (red), slowly reacting fibres to that of the quick, light fibres, to produce such interference between the waves of variation, that no difference of electrical potential at the surface remains to excite the

superposed nerve. We have in fact observed that the light fibres are much more quickly fatigued than the dark fibres.

With regard to the last point also, it can hardly be supposed that the wave of variation produced at one end of a muscle with parallel fibres, reaches every fibre at the same phase, and in this we ought to find an explanation, not merely of the vigorous excitation experienced by a nerve laid at right angles across a strong bundle of such fibres, but, still more, of the otherwise hardly intelligible secondary activity of the rectangular cross-section.

It is remarkable that during life the contracting muscles apparently exert no secondary action upon the nerves lying between them. Hering showed indeed that the twitches of the diaphragm (cat) first observed by Schiff and not explained subsequently, which are isochronous with the beat of the heart, are produced by the contact of the phrenic nerve with the beating heart. No other instance is known, and it is easier to demonstrate that under the most favourable conditions, no secondary excitation of extra-muscular nerves *in situ* results from muscles foreign to them. If the sciatic nerve is cut close below the departure of the branches to the thigh, the muscles of the leg and foot are quiescent, even with strong tetanising excitation of the same plexus, although the nerve to the leg is embedded between the much-contracted thigh muscles (Kühne). It is easy to show that this cannot be referred to the short-circuiting of the action current within the surrounding mass of muscle. Kühne always obtained secondary action when he packed the nerve of a frog's leg in the thigh, after removing the bone, and then excited the sciatic plexus, and it is well known how little other moist bodies, serving as a deriving circuit, are able to hinder secondary action. Thick layers of filter-paper, or packing the primary muscle and secondary nerve on all sides in the viscera of a female frog, produce no disturbance of secondary excitation effects. That in secondary inexcitability of the nerves *in situ* there is "a special adjustment of the muscular and nervous activity, which really accomplishes much more than is demanded by the natural conditions," seems evident from the fact detected by Kühne, that even a slight dislocation of the nerves lying between the muscles of the thigh, or their simple exposure, suffices to call out the absent secondary effect, while on closing

the wound it disappears again. With Kühne we must recognise "that the nerves *in situ* are protected against the apparently dangerous vicinity of the muscles between which they course, by the characteristic properties of the latter, which forbid them any activity relatively to each other beyond the hindering of neutralisation of the myoelectric potential in the tract through which the nerve passes" (which might perhaps be referred to the principle of interference, or exclusion of the summated action of the waves of variation).

After Hering had determined that the muscle can be excited by its own demarcation current, it was naturally presumed that it must also be possible to produce *secondary excitation from muscle to muscle*. In spite of many attempts the first experiments to this end were totally ineffective, since neither on partial excitation of a muscle were its fibres collectively, nor on total excitation were the adjacent muscles, coexcited. Kühne was the first who succeeded in obtaining secondary (pre-systolic) excitation of the frog's sartorius by the action current of the slowly beating tortoise heart, which, as we have shown, is characterised by its secondary inefficiency towards the nerves of the frog. This shows once more the extent to which secondary excitation depends on the time-relations of the current of action: the more slowly reacting muscle corresponds better with a slower wave of variation, while the quickly reacting nerve is best excited by a rapid variation. Later on Kühne succeeded, under certain special conditions, in producing secondary excitation from muscle to muscle on the skeletal muscle of the frog also.

While he never succeeded in bringing a sartorius into contraction by applying it to another directly, or indirectly, excited muscle, without pressure, the effect never fails when the muscles are partially pressed down upon one another (Kühne, 57). Under these conditions one muscle will produce secondary excitation in a whole series of other muscles, brought together by the ends, under pressure. Indirect excitation of the primary preparation from the nerve is in such a case effectual, even when the secondary excitation fails in a superposed nerve. This is especially true in regard to clonic and tonic glycerin spasms, which fail to effect any but very weak excitation in the secondary nerve-muscle preparation. This alters, however, as soon as the primary muscle is partially pressed down, when the secondary nerve, lying in the proximity

of the seat of pressure, is vigorously excited by glycerin excitation of the primary nerve. The same occurs when a second sartorius is introduced, with the press, between the first and the nerve to the leg. On the other hand, the strongest excitation induced by ammonia in the primary muscle is incapable of transfer to the secondary nerve, or to a second muscle. Direct electrical excitation of the primary muscle, which is otherwise little fitted to effect secondary excitation in a superposed nerve, is in the pressed muscle extremely efficacious in secondary excitation of the accessory muscle, even in the case in which the current is directed in the muscle from tendon to surface. Total contraction towards a localised stimulus, as well as a tendency to sustained tetanic shortening, is characteristic of each compressed muscle. The first appearance is easily explained by the secondary action from fibre to fibre, and the two work together in producing the extreme sensitivity of the partially compressed muscle: "At each impact of stimulation, when the normal muscle only reacts almost imperceptibly with a couple of marginal fibres, the compressed muscle, being prevented from twitching in bundles, shrinks together simultaneously throughout its breadth, and while the former can scarcely move a small load, the latter lifts a heavy weight, raising it while still in tetanus to a considerable height, and holding it there for several seconds" (Kühne). With regard to the constancy, or discontinuity, of the electromotive process during tetanus contraction of the compressed muscle, it is important to note that in contrast with the secondary inefficiency of the closure and opening tetanus, the strongest secondary tetanus may result, if, with excitation of the primary, partially compressed sartorius by the battery current, the secondary nerve is laid on that portion of the muscle which projects from the press. It appears from this that the tetanus outlasting excitation in the pressed muscle must not be taken for contracture, but as regards electromotive response is to be viewed as a discontinuous process, similar to that of the true oscillating tetanus with rhythmical excitation.

If any doubt still remains that there is in all these cases *electrical* coexcitation of the accessory muscle (or nerve), it is removed by the fact that the thinnest sheet of a flexible non-conductor, or metallic intermediate layer (gold leaf), prevents the appearance of the secondary excitation. Kühne, moreover,

has succeeded, though rarely, in producing secondary excitation from muscle to muscle by means of electrical conductors (salt clay), an experiment from which du Bois-Reymond obtained the first indisputable proof that Matteucci's twitch depended on electrical processes in the primary muscle. As regards the cause of the remarkable effect produced by compression of the muscle on its secondary activity, some light is obtained from experiments recently carried out *re* effect of dehydration from desiccation (Biedermann, 58).

If dead, skinned frogs, or even parts of such, are exposed freely in the air for some hours, at not excessive external temperature, they take on very remarkable properties at a certain stage of desiccation, which distinguish them in a marked degree from normal muscles, even at a high state of excitability. Here, as in partially compressed muscles, every stimulus, however localised, produces an extremely vigorous and also protracted, persistent shortening of the *whole* muscle directly affected, and in many cases of other accessory muscles also, so that energetic movements and changes of position result in these extremities, often producing an impression of reflex or voluntary movements. The excitability is not seldom heightened to such a degree that even the least shake, such as lifting the dish containing the skinless remains of the frog, suffices to throw certain muscles into persistent contraction; a gentle touch of the dry surface always produces this result. It is easy to demonstrate that this reaction in dried muscle is principally due to dehydration of the superficial layers of fibres, by moistening every point found to be sensitive to mechanical or electrical stimulation with physiological salt solution, on which the characteristic effect soon disappears permanently, although it may still be elicited in other dry parts.

If an isolated sartorius at the right stage of desiccation is placed upon a glass dish with the non-fasciculated inner side turned downwards, a series of effects can be produced by the most simple methods, which mark off such a preparation distinctly from the normal muscle, however excitable. Excitation, with a needle, of the fibres adjacent to the inner or outer margin, at any point, results, as a rule, in vigorous contraction of the *whole* muscle, so that there is no doubt that the excitation which was originally limited to a few primitive fibres communicates itself in

some way or other to the remainder. Here again, after the shortest excitation, the contraction is prolonged, and of a tetanus character analogous to that of compressed muscle.

Total excitation of the entire sartorius also occurs at the beginning of desiccation, if the muscle is partially split longitudinally (Kühne's "bifurcate experiment"), one half only being directly or mechanically excited. Both halves are then seen to contract simultaneously, and since the experiment also succeeds when the connecting bridge of muscle is barely $\frac{1}{2}$ cm. long, the purely mechanical action of the directly excited bundle of fibres upon the adjacent half could hardly be an adequate stimulus within the short tract in which it is effective. Thus there is almost complete coincidence between the response of a dried and isolated, and that of a fresh, partially compressed sartorius.

This also appears from experiments, in which the excitation is transferred from one sartorius to a second in close juxtaposition. If two suitable muscles are laid together by the broad, uninjured, pelvic ends, so that the dry outer surfaces are coextensive for about 1 cm., the two muscles react as a whole—as an excitable mass, cohering in every part, and conducting in all directions. Not merely is each excitation of the one muscle, discharged by any localised stimulus, propagated from fibre to fibre in the same muscle, but the primarily excited muscle twitching as a whole, throws the other also into secondary excitation.

It was shown that desiccated muscles behave exactly like compressed muscles, *i.e.* they respond to a short, single stimulus, not as under normal conditions by a rapid twitch, but by falling with great regularity into prolonged contracture, or a state of persistent disquietude. In the latter case the secondary muscle may be seen to follow each movement of the primary with the utmost exactness in every detail, as if the excitation were directly transmitted from one preparation to the other. The nature of secondary excitation from drying muscle to superposed nerve is also remarkable, since it tells in favour of the dictum that a rhythmical, discontinuous change of state corresponds with the seemingly continuous contracture, after a single short excitation. If the nerve of a sensitive preparation is laid longitudinally upon an isolated sartorius undergoing desiccation, the leg falls at each contracture into gentle secondary tetanus,—without reference to the nature of the stimulus, whether discontinuous excitation, or a

single short stimulus. Compressed muscle, according to Kühne (*supra*), exhibits a similar reaction.

The complete uniformity of response between desiccated and compressed muscle leads to the conjecture, that the striking tendency to secondary excitation in both cases must be ascribed to one and the same cause, *i.e. dehydration*, produced in the one instance by slow evaporation, in the other by strong pressure. It is of little consequence that the alteration which produces secondary excitation concerns the entire muscle in the one case, and only a larger or smaller section of it in the other. Kühne himself remarks opportunely that "the muscle comes out of the press as if it had been desiccated," and calls attention in another place to the "dry, dull appearance" of the pressed and flattened strip of muscle, which gives the same constant response even after removal of pressure, so that *alteration* of the muscle-substance must be held the true cause of secondary activity. In regard to excitability also, there is a general conformity between compressed and desiccated muscle, since in both cases it appears perceptibly heightened. This is indeed to a much greater degree the case with the slow loss of water by evaporation than in pressure, in which Kühne only succeeded in demonstrating an unmistakable rise of excitability in the compressed tract at the beginning, while later on, in spite of marked secondary action, it showed a significant decrease of response. For the rest the increase of excitability cannot in itself be regarded as the sole cause of secondary excitation, since it is easy to show that a much more significant rise of excitability produced in another way (effect of Na_2CO_3 solutions) does not enable the muscles to react on one another as described. Just as little can it be due to the altered time-relations of the excitation, since poisoning with veratrin, which, of course, throws the muscle into a state in which it falls into sustained contracture at the slightest stimulus, would then induce secondary excitation from muscle to muscle, which never is the case. An important point appears on the contrary from the fact that the antagonistic contact of the preparations is incomparably more intimate, when the contiguous surfaces are at a certain degree of desiccation. This may also have some application in individual muscles, where the single prinitive fibres lie in closer juxtaposition, in proportion as the muscle loses water. Still it is striking that, notwith-

standing the undoubted difference of water-content in the superficial and deeper layers of fibres in the muscle, the transfer of excitation does not seem to be confined to the former, although the direct excitation of the moister, non-fasciculated inner side is less certain to produce secondary excitation of the muscle than stimulation of the dry outer surface. This seems to indicate that the dry layers of fibres, which are the most excitable, may perhaps be distinct from the others in yet another characteristic (*i.e.* more pronounced electromotive activity). In any case many factors combine to produce this response of desiccated, or compressed, muscle.

Langendorff (59) has recently made some interesting observations, in the frog, on phenomena analogous to those of drying muscle, after subcutaneous injection of glycerin; these effects seem equally to be due to a secondary excitation from muscle to muscle caused by dehydration. If 1.5–2 cc. glycerin is injected under the skin of the back of a curarised frog, vigorous and sustained contractions appear after some time at each excitation, not merely in the same, but also in adjacent muscles, similar to those which may be observed in desiccated preparations, and doubtless to be interpreted in the same manner.

III.—POSITIVE VARIATION OF THE MUSCLE CURRENT

Hering distinguishes, in addition to the "action current" of Hermann, due to a "down" change at a led-off part, a second kind of action current caused by an "up" change of a led-off point, without any necessary "down" change at the other lead-off. If this should happen in the case of a muscle, it would obviously give rise during tetanisation to a *positive* instead of a *negative* variation of the demarcation current, due to increased positivity of the uninjured longitudinal surface, associated with upward modification. And in point of fact, certain recent observations seem to substantiate this theoretically possible event. Gaskell (60), in the first place, observed a pronounced positive variation upon the cardiac muscle of the tortoise during excitation of the vagus nerve. We subsequently succeeded in demonstrating a similar effect upon the adductor muscle of the crab's claw during indirect electrical tetanisation. As a result of a prolonged series of experiments upon the innervation and

physiological properties of cardiac muscle, Gaskell came to the conclusion that cardiac (and all other) tissue is supplied by two kinds of functionally opposed nerve-fibres, one of which (motor or accelerator nerves) he terms "katabolic," inasmuch as their presumable action is to bring about a destructive change, while the other (inhibitory fibres) he terms "anabolic," because the alterations to which they give rise are of a constructive (= assimilatory) character. Just as—in accordance with this view—"a contraction or an augmentation of muscular energy is a token of disintegration (= dissimilation), or of the activity of a katabolic or motor nerve, so is relaxation a token of integration (= assimilation), *i.e.* of the activity of an anabolic and inhibitory nerve." A similar view was previously put forth by Löwit (61) in connection with Hering's theoretical position. And already before Gaskell's work, experiments had been made (with a negative result, it is true) to determine whether the diastolic vagus-arrest of the heart is accompanied by any particular galvanic effects. Wedenski (62) by means of the telephone, Taljantzeff (63) by means of the capillary electrometer, investigated the frog's heart during vagus arrest. In the first case there was no sound, in the second case the meniscus did not move, and the absence of any kind of galvanic action seemed a legitimate conclusion. With excitation, such as to produce only a slowing of the heart's beat, and not a complete arrest, Wedenski heard a series of short sounds coinciding with the cardiac rhythm, and corresponding in pitch with the inductorium. But to attribute these to the action of motor fibres of the vagus is a very questionable proceeding. One thing is clear enough—it is hardly practicable to devise a convincing experiment upon the possible galvanic effects of vagus excitation, while the normal rhythmic action of the heart persists; on the other hand, it is no easy matter to obtain a prolonged arrest of the heart without considerable interference with its anatomical and functional connections. Nevertheless Gaskell has succeeded upon the tortoise heart in obtaining a preparation that corresponds with an ordinary nerve-muscle preparation in that the muscle is at rest—the nerve, on the other hand, being an *inhibitory nerve*. In the tortoise and the crocodile a particular nerve (the "coronary nerve") runs alongside of one of the coronary veins, from the sinus venosus to the aortic bifurcation.

This nerve, together with the sinus, can be completely isolated from the remainder of the heart, when it forms the sole channel of communication to the auricle which, with the ventricle, is separated from the sinus. After the separation has been made, both auricle and ventricle remain completely quiescent, and only resume pulsation later, so that the experiments can be effected during the quiescent period. To this end the apex of the auricle is burned, yielding in consequence a strong demarcation current, when the leading-off electrodes are in contact with the thermic section and the uninjured base. Like the ventricle current, this auricle current declines rapidly at first, then more slowly. *During this time each vagus excitation gives rise to a positive variation*, which begins quickly, reaches a maximum in about 10 secs., and at cessation of excitation sinks with increasing rapidity, so that after 18–20 secs. the magnet takes up the position which it would have occupied in the absence of vagus excitation. There can be no doubt that this effect depends upon changes that have arisen in the uninjured part of the auricle, and are “accompanied by increased positivity of that part, just as contraction of the auricle is accompanied by diminished positivity of uninjured tissue.” If the auricle now recommences to beat, each contraction gives rise to a *negative variation* of the demarcation current, far larger, as a rule, than the positive variation; cases, however, occur in which both kinds of variation are about equal in magnitude—yet even here there is a very characteristic difference with regard to rapidity of decline in the two effects. The swing back of the magnet is far more rapid after a negative than after a positive variation. If the excitation of the vagus is continued for any length of time, the positive variation may subside completely, even during the excitation. These galvanic effects of the vagus, like its inhibitory function, are abolished by atropin poisoning.

As is well known, the heart is influenced not only by inhibitory, but also by antagonistic, viz. excitatory, nerve-fibres, which suggests the possibility of obtaining opposite galvanic effects by excitation of the latter. And Gaskell, in fact, has succeeded under given conditions in obtaining a negative variation of the quiescent ventricle (64).

We ourselves performed experiments on the innervation of the claw-muscles of the crab (65), the results of which will have

to be discussed more fully later on, but which showed that in this case also, each of the two antagonistic muscles is, like the heart, subject to the influence of two functionally different kinds of fibres (inhibitory and excitatory), which run in the same nerve-trunk, and are capable of eliciting opposite mechanical effects. It was natural to suppose that opposite electromotive effects, in correspondence with this antagonism, would obtain in the form of negative, or positive, variations of the muscle current. But there were considerable difficulties in the way of experimental investigation; in the cray-fish, at any rate, it is not possible to isolate the nerve in a state of excitability, while the muscle must be left within the shell; this, if for no other reason, is imperative from the mode of origin of the component fibres, which spring from a large portion of the inner surface of the last segment of the claw, and for the most part converge to the tendon. The disposition is thus very similar to that of the tendinous expansion of the frog's gastrocnemius. At whatever part of the base of the claw the shell is opened, an artificial transverse section of the muscle is inevitable, and it is nowhere possible to expose the uninjured surface (natural longitudinal surface) alone. Under these circumstances the most advisable proceeding is to lead off from an injured part within that area of the claw at which fibres of the adductor muscle take origin (the particular position of this led-off point is in general of no consequence), using as a second lead-off from the uninjured muscle some portion of the electrically indifferent tissue that occupies the interior of the hollow limbs of the claw, and may to some extent be regarded as a prolongation of the tendon. To this end a small piece of the shell, preferably near the base of the claw, is broken off from the outer edge, towards either the outer or inner surface, by bone-forceps. A second smaller opening is made at about the middle of the outer edge of the fixed limb of the claw—the small adductor muscle having previously been completely removed—to serve as the second lead-off of the demarcation current, while the free limb of the claw serves to indicate any movement due to altered action of the adductor. The exciting electrodes (platinum points) transfix the longest segment of the claw extremity near its outer border. With this disposition the lead-off nearer to the base of the claw is of course negative to the distal lead-off.

If the claw-nerve is now tetanised (the demarcation current having been previously compensated), the usual effect with the gradual approximation of secondary to primary coil is a more or less considerable deflection in the direction of a positive variation of the demarcation current, followed by a diphasic (negative followed by positive), and finally by a simple negative deflection. As a rule the positive deflections are smaller than the negative deflections. With regard to the time-relations of the positive variation, it may be remarked that the variation, as a rule, follows close upon the commencement of excitation, and very gradually diminishes during its course. Owing to the fact that the adductor muscle is frequently in a more or less pronounced state of tonic contraction (which, as will be shown later, may be abolished by weak excitation of the nerve, whereas strong excitation always augments, or initiates contraction), it seems natural to bring the galvanic changes into direct causal relation with the simultaneous alterations of form in the muscle. No such parallelism of the two orders of excitation effects can, however, be predicted. It frequently appears that the electrical effect is still purely positive, or diphasic, while the muscle is already in tetanus. Nor is it rare to find cases in which the adductor muscle contracts vigorously with a certain strength of excitation, while the electrical changes are quite insignificant, there being either a visible antagonism of effects, or no perceptible result, positive or negative. In such cases, strong currents, as a rule, produce negative deflections in one direction only, usually insignificant in magnitude, and followed by a strong positive after-effect when the excitation is over. Minimal galvanic effects, or complete failure of action, frequently occur in animals which have been exposed for some time to a very low temperature ($0-5^{\circ}\text{C.}$). In other cases, under the same conditions, the positive variation is well marked and vigorous. On the whole, the experimental results obtained vary to a surprising extent in different, though apparently similar, crabs. In single cases it was found possible to obtain positive effects in one direction only, with any given strength of excitation after very strong doses of curare, although the muscle goes into tetanus after each stronger excitation, so that there is no question of complete curare effect. After poisoning with curare the positive variation is always strongly developed in

comparison with normal preparations, even if deflections in the direction of the negative variation occur on increasing the stimulus. Eventually we obtained pure positive effects in one direction by the application of a simple device, viz. fatiguing the adductor muscle by unilateral exertion, until the reactions from the *motor* nerves of the claw were reduced to a minimum.

In fresh, lively crabs it is easy to fatigue the adductor muscle in a comparatively short time to such a degree that voluntary or reflex contractions are only possible to a very limited extent. It is only necessary to excite the muscle into vigorous contractions, repeated as often as possible, by means of continuous stimulation of the animal (insertion of a firm body and finger between the joints of the claws). The extraordinary strength and duration of the first contractions diminish with surprising rapidity; longer and longer pauses are required before the crab can be stimulated to renewed, effective contraction of the claws, and finally even painful excitation ceases to produce it.

If a preparation thus fatigued is tested as above in regard to its electromotive activity during excitation, it will be found without exception that *every trace of a negative variation is wanting, while strong positive deflections accompany each effective tetanisation of the nerve.* The effect begins in different animals within a tolerably wide range of current, increases to a certain limit with approximation of the secondary and primary coil, to decrease again, as a rule, with further increase of stimulus; this effect may perhaps be referred in part to an interference of the two opposed effects of excitation, as is indicated *inter alia* by the fact that at a lower degree of exhaustion of the adductor muscle every possible transition occurs between diphasic action with a predominance of positive deflection, decreasing in size with increasing strength of current, and simple positive variation.

The independence of the galvanic effects of excitation from any simultaneous change of form in the muscle, is quite unmistakable in these experiments. In many cases mechanical effects still appear in a fatigued preparation when it is strongly excited from the nerve, and are expressed in a shortening of the adductor muscle, which, however, is then accompanied, not by a negative, but invariably by a positive variation of the

muscle current. In other cases again, all change of form is wanting in the muscle, even with the strongest excitation, while, on the other hand, the positive variation comes out in apparently undiminished proportions. We observed the same phenomenon in the adductor muscle of a crab, in which all the muscles had undergone pathological change, and looked gray, as if from boiling. These experiments show definitely that a positive variation of the muscle current may appear in consequence of nerve excitation, not merely when the muscle in tonic contraction relaxes, but also when it is free from tonus and exhibits no change of form on excitation, or even shortens slightly. With regard to the time-relations of the positive variation, it must be observed that the beginning of the deflection coincides, as a rule, with the beginning of excitation, so that in prolonged tetanus of the nerve the scale remains some time at maximal deflection; when the circuit is broken it returns to its position of rest with declining rapidity, but fails (in the initial excitations) to reach it completely, so that the muscle current at first increases steadily in consequence of nerve excitation.

If a preparation which is in such a state that every effective excitation produces only a positive variation of the muscle current, is kept for a long time at a low temperature, and the effect of exciting the nerve is periodically tested, it is found that the deflections under similar conditions, with uniform strength of coil and duration of closure, are gradually lessened, and even change their sign under certain conditions,—since with strong excitation a weak negative variation appears again, either as the prelude to a stronger positive variation, or independently. Thus, after a long rest, a fatigued muscle preparation may return more or less to the normal, characterised by diphasic galvanic effects of excitation. The changes referred to are independent of the simultaneous diminution of the muscle current, which may easily be excluded by further supplementary injury to the parts of the muscle still uninjured. If, as has just been stated, it is possible to throw the adductor muscle of the crab's claw by prolonged and exhaustive activity from *the central organ* on the one hand, and on the other (though less certainly) by poisoning with curare, into a state in which tetanisation of the corresponding nerve produces only a positive variation of the muscle current, it is still easier to exclude this last effect entirely, and, under

uniform conditions of experiment, to produce a *negative variation in only one direction*. This is readily understood when we remember that the negative effects preponderate greatly under normal conditions, while the opposite positive variation appears properly at a very limited range of the scale of excitation, while later on it is masked completely. In order to abolish it altogether, it is only necessary, as a rule, with even weak excitation, to keep the animals under experiment for several hours in water at 20–25° C., or to leave the claws, cut off, for some time (about an hour) in a moist chamber at normal temperature. The adductor muscle then exhibits an electromotive reaction to excitation from the nerve, which is the exact opposite to that of continuous activity. While the muscle thus exhibits a negative variation in one direction only, both with the minimal excitation from the nerve, and with maximal currents (*i.e.* responds, like all other known voluntary, striated, vertebrate muscles), the same muscle, under uniform conditions of excitation and leading-off, will sometimes yield precisely opposite electrical changes, expressed in a positive variation of the demarcation current,—which have so far found an analogue only in vertebrate cardiac muscle. These two opposite variations of the muscle current exhibit certain striking peculiarities, as regards both strength and time-relations, when they appear as the sole effect of excitation under the above conditions; and these are not without importance in the interpretation of the phenomena. In the first place, it is found that in the one case, as in the other, the magnitude of the deflections on the galvanometer is nearly always greater, at uniform conditions, than it is in a perfectly fresh normal muscle of a “cold crab.” In such a preparation the effect in one or the other direction is seldom more than 50 degrees of the scale, while in a fatigued adductor muscle the positive deflections frequently amount to 100 divisions of the scale, and the negative effects in preparations of “warm crabs” are still more striking.

In the normal adductor muscle again a prominent fact is the rapid swing back of the negatively deflected magnet, on the prolongation of strong excitation, although, as is easily proved, the tetanisation of the muscle persists much longer. Not infrequently the scale flies beyond its zero, and remains deflected in the sense of an opposite positive variation. A preparation that

has been previously heated gives quite a different reaction; the negative variation in this case quickly reaches its maximum, and only diminishes slightly if the excitation of the nerve continues. The magnet only returns to rest when the circuit is broken. The effect is therefore similar to that in striated vertebrate muscle. We have stated above that the positive variation of the fatigued muscle tends at first to a permanent increase of the demarcation current, while later on, with repeated excitation, it compensates itself each time slowly, but completely. A negative after-variation, such as is often observed on strongly curarised preparations, is regularly absent in fatigued muscle.

The next question connected with the appearance of the positive variation on indirect tetanisation of the adductor muscle is whether there is here a discontinuous alteration of state in the muscle-substance, as in the negative variation which otherwise accompanies excitation. We have unfortunately not been able to decide this point from frog's nerve-muscle preparations, since, under even the most favourable conditions, it seems impossible to elicit secondary twitch, or secondary tetanus, from the adductor muscle. Investigation of these effects by means of the capillary electrometer, which we have not yet been able to carry out, might here also give the desired solution. In the light of other observations on the same preparation—to be discussed below—the experimental results point to an explanation, which is directly connected with Gaskell's theory, as above quoted. Remembering that the adductor muscle of the crab's claw is supplied, demonstrably, by two functionally distinct nerves, inhibitory and excitatory (assimilatory, dissimilatory), which on excitation produce opposite changes of state in the muscle-substance (expressed by antagonistic changes of form on the one hand, and by contrary electromotive action on the other), it must be assumed that the galvanic effect observed with a moderate intensity of the artificial stimulus to the nerve is, as a rule, the result of co-operation between two contrary and simultaneously excited processes, the alternating ratio of which depends on the one hand on the strength of excitation, on the other on the temporary condition of the muscle.

The strongest argument in favour of a masked diphasic response—even in such galvanic effects as, with strong excitation of the normal adductor muscle, yield experimentally negative

deflections in one direction only—derives from the remarkable variations in magnitude exhibited under approximately equal conditions. This affords a *prima facie* explanation of the striking fact that the galvanic effects of excitation are often insignificant, even in preparations made from fresh, vigorous animals, and may fail altogether at a certain medium strength of current. This must indeed follow inevitably, where the two antagonistic processes terminate simultaneously as regards the electrical changes which they effect in the muscle. Finally, both the diphasic action and the interference phenomena before alluded to (positive after variation and oscillation of the magnet to a new equilibrium) conform with the above theory. If we are to explain the monophasic, but antagonistic effects, of minimal and maximal excitation, we must assume in the first case a more prompt reaction of the inhibitory (assimilatory) processes, in the other a preponderance of the process initiated in the muscle by the exciting (dissimilatory) fibres.

Moreover, we find experimentally that no artificial excitation of the nerve produces that state of fatigue in the muscle in which it is characterised by a special disposition to positive galvanic effects, while these never fail to appear when fatigue is induced by natural excitation of the nerve from the central organ. This difference is intelligible on the assumption that in the last case the exciting fibres are alone, or mainly, involved, while in artificial excitation both kinds of fibres are necessarily excited simultaneously, so that the resulting changes of the muscle in either case must be dissimilar.

And lastly, we must emphasise the fact that in indirect excitation of the adductor muscle the galvanic effects are by no means in such close relation with the mechanical effects of excitation as might be concluded from countless experiments on vertebrate nerve-muscle preparations. Rather, as has been shown, there is a fundamental independence of the two, since notwithstanding the marked contraction of the muscle, the galvanic effects of excitation are but slightly developed under some conditions—although in the right direction (negative variation)—while at other times they fail altogether, or appear as a positive variation. From this we must conclude, in view of the preceding observations, that *the antagonistic relation of the two processes simultaneously excited in the muscle may bear a different value*

with respect to the mechanical effects of excitation and to the electromotive reaction; since here the consequences of excitation, and there of the simultaneous inhibition, preponderate, or are alone manifested.

We must further point out the analogy between this reaction of the adductor muscle and the observations of Fano on the cardiac muscle of the tortoise, where, also, there is imperfect correspondence between the changes of form in the muscle and its simultaneous electrical manifestations (66).

IV.—SECONDARY ELECTROMOTIVE ACTION IN MUSCLE

In muscle (as in nerve, electrical organs, and irritable protoplasm in general) the passage of the electrical current is followed by certain electromotive reactions, which are intimately related with the action current, and are to a certain extent only a special form of its manifestation. As early as 1834, Peltier discovered that frogs' limbs, or isolated muscles, or even pieces of muscle, developed a current in the reversed direction.

Du Bois-Reymond (67), who took up the investigation later, convinced himself that the secondary current (after-current) is not exclusively, if at all, dependent on the polar zones, but is also initiated in the tracts lying between them, since he found that any given section of the intrapolar tract of a muscle traversed longitudinally gave an electromotive response in the same direction, on opening the polarising current; accordingly he advanced the view that this effect mainly depended on so-called "*internal polarisation*."

Many inorganic and organic porous bodies, saturated with an electrolyser, do actually possess the property of acquiring *negative* internal polarisation. The polarising current then divides itself between the badly conducting, saturating fluid, and the porous vessel, the latter being polarised from the zones. "Each of the countless intermediate points now gives an electromotive reaction in the reverse direction from that in which it was traversed by the current." The superposition of all these partial currents results in the branch current, which passes through the deriving circuit. Each coextensive tract in any such regularly constructed prismatic, or cylindrical, body gives, as a rule, a strong secondary electromotive reaction after the passage of the current.

It was soon observed that living muscle, traversed by current, behaves in this respect very differently from dead organic, or inorganic, bodies, more especially in that positive, as well as negative, after-currents appear under some conditions. For the investigation of polarisation effects in muscle, du Bois-Reymond generally used the gracilis and semimembranosus muscles, stretched conveniently. A pair of non-polarisable electrodes on each side served to lead in the polarising current, and to lead off the polarisation current. The second pair were usually placed between the others, within the intrapolar area. A special contrivance made it possible to alter the "period of closure"—*i.e.* the time during which the polarising current was sent through the object to be polarised—from 0.001 to 20 secs. The same contrivance effected closure of the galvanometer circuit after breaking the battery circuit at a minimal and constant interval.

The secondary electromotive effects observed under these conditions of experiment in the muscle are essentially dependent on the density and duration of the primary current, while they are much confused from the persistent interference of negative and positive action. "With a current density lower than that of two Groves, and with quite a short closure, no polarisation is, as a rule, perceptible in the galvanometer. The first traces found with one Daniell and 1 sec. closure are negative. The first positive traces, on the other hand, first appear with two Groves, and about 0.3 sec. closure."

With an increasing period of closure, du Bois-Reymond found that the positive polarisation quickly reached its maximum, to decrease more slowly, and pass over into negative polarisation, which on its side again rises to a maximum. He fixes the "critical point" of closure as that at which positive passes into negative polarisation. The strongest positive polarisation in these experiments was at a closure of 0.0075 secs. with 20 Groves (!), the strongest negative polarisation at 10 minutes' closure of 1 Grove. Short impacts of current (induction shocks) produce only positive polarisation.

Both positive and negative polarisation are very persistent, and sometimes outlast the opening of the polarising current for 20 minutes or more. If they are initiated at the critical point, du Bois-Reymond not infrequently observed a diphasic variation,

corresponding usually with first a negative and then a positive polarisation. This is due to the fact that from the moment of closure onwards, *both* kinds of polarisation are simultaneously present, but increase in different proportions, "negative polarisation increasing more in ratio with the time of closure, while the positive variation is augmented quickly at first and then more slowly."

Du Bois-Reymond further concluded from experiments in which the upper and lower half of regular muscles were alternately traversed by the current, and tested for polarisation, that "strong positive polarisation is exhibited in the upper half in an ascending, in the lower half in a descending, direction." Dead muscles still exhibit *traces* of negative internal polarisability which is completely abolished only by boiling; positive polarisation, on the other hand, is exclusively characteristic of living muscle. Du Bois-Reymond concluded that "it is not electromotive forces, homodromous with the primary current, which are generated by the positively polarisable tissues, but the carriers of electromotive forces already present (electromotive molecules) which are homodromously adjusted with the primary current."

How little these results really go to support the molecular theory, however, is strikingly obvious in the later investigations of Hering and Hermann (68-69). Hering proves conclusively that there can be no question of *internal* positive or negative polarisation in a longitudinally traversed muscle in du Bois-Reymond's sense, since the actual seat of the electromotive changes induced by the exciting current lies at those points of the contractile substance by which the current enters or leaves the muscle (the physiological pole), so that the close relation between these phenomena and the polar effects of current is unmistakable.

If, in the same sense as above, we regard every change in the chemical activity of any part of the muscle-fibre as the *sine qua non* of the appearance of electromotive action, we shall premise that on sending current through a muscle with parallel fibres, the chemical alteration of the contractile substance recurring presumably at the physiological kathode and anode will initiate differences of potential, which must be discovered when one or other end so altered of the muscle is led off in connection with a point of the unaltered surface of the muscle. The results

obtained by Hering from such experiments on the frog's sartorius actually correspond throughout with this assumption.

If the muscle is fixed at moderate tension, and current sent through it from the stumps of bone on either side, on leading off from one or the other tendon-end, and from a point on the longitudinal surface, the muscle current measured previous to excitation is found on opening the circuit to be considerably altered, *i.e.* increased, diminished, neutralised, or reversed, in correspondence with the direction, strength, and duration of the exciting circuit, and the strength and direction of the original muscle current. If the muscle current has previously been compensated, positive or negative increase of the "polarisation currents"—corresponding with the muscle current—will appear, and may be positive or negative, *i.e.* parallel with the exciting current, or opposed to it in direction. Since these have their real origin in the anodic and cathodic points of the muscle-substance, Hering distinguishes between *anodic* and *cathodic* polarisation. The former may be either positive or negative, according to the strength and duration of the exciting current, the latter in the majority of cases is negative only.

With a short closure, very weak currents invariably yield a negative polarisation current in fresh muscle, so long as only the anodic tendon-end, and a point at about the middle of the muscle surface, are in circuit. With stronger excitation currents, on the other hand, and not too brief closure, *positive* polarisation only results, which increases with the strength of current, and finally far surpasses the strongest negative anodic polarisation.

Very strong currents produce positive polarisation, even with minimal closure, while weaker currents, with short closure, excite negative, or diphasic (first negative, then positive) polarisation, and produce a positive effect after prolonged closure only. Induction currents also cause a similar reaction to strong constant currents, with minimal closure, since they only produce positive anodic polarisation.

All these polarisation effects (after-currents) are wholly wanting, or appear as a trace only, if both leading-off electrodes are applied to the longitudinal surface of the muscle, without being too close to one or the other end of it.

Since, according to Hermann's alteration theory, excited muscle-substance is negative towards unexcited substance, there

can be no doubt (in view of the conditions and behaviour of the break excitation in muscle) that positive anodic polarisation is an expression of the same, *i.e. the positive polarisation current produced by alterations of anodic points of the contractile substance is an action current due to the break excitation from the anode*; an action current which behaves very differently from the action current produced by the make excitation that has so far exclusively concerned us.

The long persistence of negativity in the anodic points is most remarkable; it is easily explained by the fact that the opening of a constant current under some conditions leads to protracted excitation (persistent opening contraction) of the muscle. This gradually declines, being more and more confined to the anodic points of the muscle. But even when, as on sending in weaker currents, or with a shorter duration of strong currents, there is no visible persistent break contraction, or even break twitch, there is nothing to prevent us from regarding the positive polarisation current in question as the expression of opening excitation lasting for a considerable period,—since a low degree of contraction is difficult or impossible of demonstration, especially when it is confined to the immediate vicinity of the anodic or kathodic points of the muscle, and since, moreover, negativity may be present as the expression of excitation, without any trace of contraction.

Hermann's view of the positive anodic after-current only differs from that of Hering inasmuch as, starting with the assumption of an intrapolar electrotonus, he derives the action current at break from the whole anelectrotonic tract of the muscle. We have already seen, on the contrary, that if the currents employed are not too strong, all the changes which can collectively be termed "electrotonus" are strictly confined to the physiological electrode points.

Kathodic polarisation is almost exclusively *negative* in striated muscle. It first appears on leading off in the sartorius, through which current is passing, from the kathodic end and centre of the muscle, with very weak currents, after a closure of several seconds, increasing steadily with increase of current and longer closure. If it is compared with the positive anodic after-current which appears at the same end of the muscle, with equal strength, and duration of closure, the latter soon becomes by far

the stronger. With very strong currents and long closure, the negative kathodic polarisation may become as strong as the equally abterminal muscle current which shows itself—the electrodes being unaltered—on killing the end of the muscle. Induction currents, too, give negative kathodic polarisation, but it is essentially weaker than the positive anodic polarisation produced by the same strength of current on the same muscle (*sartorius*). The conclusion therefore is that with growing strength and duration of the exciting current, the kathodic region of the muscle (physiological kathode) becomes increasingly more negative in comparison with the centre. If this were an equivalent phenomenon to those of physical, internal polarisation, the negative polarisation current would—as has been shown—necessarily appear in approximately equal proportions on leading off from any point of the interpolar tract, and this, as Hering shows, never is the case. When the two galvanometer electrodes are placed at the margin between the upper and middle third of the *sartorius*, the exciting current being led in as before through the bones, no polarisation current can be observed, or it is so insignificant as compared with the anodic and kathodic polarisation that it may practically be neglected. The relatively weak effects in the interpolar tract on the application of very strong currents, with prolonged closure, are sufficiently explained by the fact that the polar points of the muscle are never limited exclusively to its ends,—due *inter alia* to the fact that the *sartorius* not infrequently exhibits short fibres which end, or begin, somewhere in the length of the muscle. On the other hand, the appearance of persistent opening and closure contraction of course produces inequalities in the individual parts of the interpolar region. There is thus no reason for assuming internal polarisation of the muscle-substance in du Bois-Reymond's sense. *All the phenomena of negative kathodic polarisation can be referred to chemical alteration (excitation, or local fatigue) in the kathodic points of the fibres collectively.*

Nor are the later experiments of du Bois-Reymond more convincing, in which the application of a current of ten Grove cells to the curarised *sartorius*, produces after 15–25 minutes' closure “a secondary electromotive force in the reverse direction to the polarising current in every tract of the muscle,” its magnitude increasing with the length of the tract led off. For the

extent to which the excitability and conductivity of the muscle is altered by such impossibly strong currents is sufficiently attested by the appearance of the galvanic wave under these conditions, as well as by the persistent excitation (often excessively marked and widely distributed over the intrapolar muscle tract), in the region of the anode, which depends, as was shown above, upon the effectuation of secondary electrode points. But there can hardly be a question, after the foregoing discussion, that experiments performed under such abnormal conditions in no way contravene the clear and simple result of Hering's investigations.

The most striking proof that secondary electromotive phenomena are pure *polar* effects of current is, however, the fact that killing the anodic or kathodic points of the muscle hinders the appearance of both positive and negative kathodic polarisation, exactly as occurs in the opening and closing excitation. The negative, and still more the positive, polarisation current thus implies integrity of the kathodic or anodic points of the excitable substance.

Hermann pointed this out in regard to the positive anodic after-current in muscle, designating it in consequence an "*irritative*" negative after-current, *vs.* that "derived from true polarisation." Like du Bois-Reymond, he derives the latter from the whole interpolar tract, and, after partial passage of current, from the extra-polar region also, in consequence of a polarisation, which he takes to be equivalent with certain polarisation phenomena (*infra*) that occur in medullated nerves, and can be reproduced upon a polarisable wire surrounded by an electrolyte, through the sheath of which the current enters. He finds that the effects upon this ("core") model coincide with the polarisation phenomena, both inter- and extra-polar, of muscle and nerve, the "polarising after-current" being in the first place heterodromous, in the second place homodromous, with the polarising current.

We shall enter more fully into these relations when discussing the electrical excitation of nerve; for the present it is enough to say that just as these effects are indisputable under certain conditions, so too in muscle, within a given "physiological" range of strength of current, the negative kathodic must, equally with the positive anodic, be designated an "irritative" after-current, due entirely to polar current action.

The earlier, and contrary results of du Bois-Reymond are, as Hering showed, to be referred to the fact that he employed two muscles, one of which was entirely, the other at least partially traversed by a tendinous intersection. On leading off from two points of the interpolar tract, there must as a rule be countless anodic and kathodic points between the contacts of the leading-off circuit, more especially when the tendinous wall of partition (running obliquely to the muscle axis, and dividing each of the two muscles so as to form two separate muscles lying one behind the other) falls completely within the two galvanometer electrodes. In front of the intersection the current leaves by the fibres of one of these separate muscles, to enter again by the fibres of the second. On one side of the intersection therefore there are countless kathodic, on the other as many anodic, points, and both are the seat of polar changes.

Here too du Bois-Reymond has recently tried to give another interpretation from the standpoint of the molecular theory, but it is so obviously inadequate that he himself recognised its great difficulties, which are not removed by a whole series of accessory hypotheses. The polarisation effects in the gracilis muscle are derived by this theory—tested on a “clay dummy” (consisting of a round clay stamp, hollowed out in the centre, with the patellar tendon of a frog clamped between its two halves)—from “an axially directed, antagonistic force, initiated in each superficial element of the intersection.” Experimental observations, however, did not correspond with the theoretical response of the muscle, and du Bois-Reymond was compelled to adopt the theory of a “false internal polarisation,” for which no explanation is given. The palelectronic tract, or layer, on the other hand, is the seat of “true” polarisation at the ends of fibres. Du Bois-Reymond, however, considered it impossible to refer this to the negative variation, because “no such relation seems to obtain between the mechanical effects of excitation and polarisation, as must exist if polarisation is to be conceived as the after-effect of negative variation, or as the negative variation proper.” He therefore takes no account of the fact that such complete parallelism exists just as little between the *visible* effects of the opening excitation and the positive anodic after-current, although there can be no doubt as to the causative connection between them. Du Bois indeed goes so far as to deny the presence of per-

sistent excitation in the sartorius, on the strength of experiments similar to the polarisation experiments. This is not the place to enter further into the discussion, which may be referred to Hering's recent criticism (68).

At first sight an argument in favour of du Bois-Reymond's view, and against that of the positive anodic after-current as the galvanic expression of the opening excitation, might be deduced from the fact that these effects of the passage of current appear equally when the muscle is in deep ether narcosis, a condition in which the strongest excitation fails to produce any trace of visible change of form. Thus it would seem as if the *local* capacity of reaction in the muscle were not perceptibly affected by narcosis (as far as may be judged from the galvanometric changes visible); since the capacity of the muscle to yield a positive anodic after-current, when stimulated by the electrical current, is not merely unimpaired by protracted treatment with ether, but is even considerably augmented—it subsequently remains constant for some time, and only diminishes perceptibly at a much later period. If the negative kathodic polarisation of the etherised muscle is similarly investigated, it is also found to undergo no diminution during narcosis.

In both cases, however, the appearance of the after-current is affected or totally hindered, as under normal conditions, on killing the anodic or kathodic ends of fibres. In place of the positive anodic polarisation, a much weaker, negative after-effect may then be observed, while no trace remains of the negative kathodic polarisation, even with prolonged closure.

The idea of excitation is so closely allied in the muscle with that of active change of form, or at least the possibility of the same, that the hypothesis of a prolongation of excitability when contractility has been entirely abolished, encounters *a priori* difficulties. Secondary electromotive manifestations appear indeed in a rigidly stretched muscle, but then both conductivity and the negative variation are still present, and the muscle would contract *in toto* if not mechanically hindered. The ether muscle, on the other hand, has not only completely lost its power of shortening on excitation, but has also become wholly incapable of conducting. The great majority of experiments in muscle and nerve physiology, however, justify us in assuming a close relation between conductivity and excita-

bility, although on the other hand the changes in the two functions do not always keep pace, and the one faculty may be already abolished while the other is still in existence. We need only in this connection refer to the fact that in the process of dying, the manifestations of contraction which appear with mechanical or electrical excitation become more and more confined to the seat of direct stimulation, where they are still energetic when conductivity has been entirely arrested ("idiomuscular contraction"). This is generally explained on the assumption that the conductivity of the muscle disappears, with diminishing excitability, before its direct capacity for response. The same thing may be observed in the course of ether narcosis also, since electrical excitation in the region of the kathode still produces a plain contraction; although on exciting one end and leading off from the other no trace remains of any negative variation of the demarcation current, *i.e.* conductivity is almost entirely abolished. In view of these facts it is natural to ask whether the continuation of polarisation effects might not be referred to exclusive localising of both opening and closing excitation to the extreme ends of the muscle-fibres, the shortening of which might easily escape undetected. No such effect, however, is indicated by microscopic observation of the muscle traversed by current, and it may be assumed that with sufficiently prolonged etherisation all perceptible trace of local contraction disappears (in excitation with the electrical current), although the polarisation effects in question may be observed in full vigour before as well as after. We may conclude therefore that *the manifestation of the changes which underlie the after-current is quite independent of the persistence of contractility and conductivity.*

This does not, however, exclude the view by which positive anodic, and negative kathodic, after-currents are regarded as the consequences of break and make excitation, but may be brought into agreement with it, if the possibility of localised excitation without simultaneous change of form in the muscle is admitted. This possibility is the less to be doubted since the same phenomena also appear under perfectly normal conditions. We need only refer to the fact that with direct electrical excitation of the muscle there will always be a limit of strength of stimulus below which the current no longer

discharges perceptible mechanical excitation effects, although it still works changes in the muscle-substance which are expressed in other ways, more especially by an alteration of excitability at the points of entrance and exit. Further, it is known (as Hering pointed out) that the break excitation may be identified on the galvanometer as a positive anodic after-current, "even where this is not visible to the eye, nor even perhaps microscopically." At all events there are excitations which must be termed subliminal as regards change of form in the muscle, while in a narcotised muscle the strongest excitation fails to develop any directly visible reaction. These facts make it clear that the relation between contraction and excitation is by no means so immediate as might *a priori* be supposed, but that the indirectly demonstrable changes in the muscle-substance may occur in consequence of previous excitation, without perceptible changes of form. And it is very remarkable in the etherised muscle that the polarisation effects described show no perceptible weakening throughout the entire period of narcosis. This tells in favour of the fundamental independence of excitability in the muscle from its contractility and conductivity.

Under these circumstances it is the more interesting that the possibility of excitation seems to exist in another and different alteration of the muscle-substance, in which contractility is equally more or less affected. In this case it is not merely the polarisation phenomena under discussion that continue, but (where the changes that occur are local, and confined to the seat of direct excitation) there are also changes of form in the normal section of the muscle. We have already seen that striated muscle is capable of taking up a considerable bulk of water without losing its capacity for electromotive response, when irritated, as under normal conditions. If the water treatment is confined to one or the other end of a sartorius, this end may in consequence of imbibition undergo great alteration in its physical properties, without, as we have seen above, becoming negative to the uninjured part of the preparation. This agrees with the fact that excitability towards the electrical current is not perceptibly affected, if it is sent through the muscle in such a way that the point of direct excitation is situated at the altered end of the muscle. This is found on the one hand from comparing the height of twitch, on the

other from the behaviour of secondary electromotive phenomena before and after local treatment with water. The mechanical, like the galvanic, effects of excitation are invariably altered in the same way (provided the point of direct excitation coincides with the injured end of the muscle) by every kind of stimulus, localised application included, which produces radical injury of the chemical properties of the muscle-substance: we are therefore forced into the conclusion that the excitability of the swollen section of the fibre does not at first suffer perceptibly in the case under consideration. On the other hand, there is no doubt that its contractility diminishes considerably in consequence of the rigor-like condition of the muscle, even in the earliest stages of the water effect. When, notwithstanding, not merely the continuance of the positive anodic, and negative cathodic after-currents, but also vigorous make and break twitches, are observed on sending current in or out at the end treated with water, we must inevitably conclude that capacity for active change of form at the seat of direct excitation is not essential to excitability in the muscle. It follows that the complete loss of contractility in the etherised muscle can, as little as that of conductivity, be regarded (under similar conditions) as a valid objection to the interpretation of polarisation phenomena—and of the positive or anodic after-current in particular—as the effect of excitation; the less so since the same facts which tell most decidedly in favour of the view in question can be observed as well on an etherised as on a normal preparation. This applies particularly to the consequences of injuring the ends of the fibres. In every case it may be demonstrated that the appearance of the positive after-current is rendered impossible when the anodic end of the muscle has been killed by any means whatever.

The results of this discussion may be summed up in the proposition that *striated muscle under the influence of ether vapour falls into a condition in which the application of an external stimulus produces no directly perceptible changes whether localised at, or distant from, the seat of excitation; while, on the other hand, galvanometric changes, of equal strength with those produced before narcosis, do appear demonstrably at the point of excitation, although in consequence of the abolition of conductivity they are only locally evident.*

The category of secondary electromotive phenomena is not completed with the admission of positive anodic and negative cathodic polarisation in striated muscle. In view of the striking *polar inhibitory effects* exhibited under certain conditions, not merely in tonically contracted smooth, but also in striated muscles under the influence of the battery current, it is evident that the effects of electrical excitation of such a muscle must, in regard to secondary electromotive phenomena, express themselves sometimes—under given conditions—as positive cathodic, or negative anodic, after-currents. And, in reality, if a muscle with parallel fibres is conceived as uniformly excited (contracted) in all its parts, it will be as ineffective in external electromotive response as in the wholly uninjured state; if it is then traversed longitudinally by current, relaxation occurs during closure at the anode, due to quelling of the existing excitation, while at the kathode there will subsequently be an increase of contraction. On opening the circuit everything is reversed, and the inhibition is localised at the kathode. Then, if we picture the corresponding end of the muscle as connected with the centre by a leading-off circuit, current would flow in the same from end to middle—in the muscle therefore in the reverse direction, *i.e.* in that of the polarisation current, *i.e.* positive (70).

Just as the polar inhibition of contraction is best exhibited in veratrin poisoning, it is easy by the same method to investigate the galvanic changes produced by the electrical current in a strip of muscle, alternately resting and excited. Instead of poisoning the whole muscle with veratrin, it appears in this case better to apply it to one end of the sartorius only. Each momentary excitation will then, as has already been pointed out, induce pronounced and tolerably protracted negativity of the poisoned strip. If the lower end of the sartorius is taken, and closure of a descending battery current (2 Dan.) effected for a short time (1–4 secs.), after rapidly compensating the veratrin action-current developed by a brief excitation, there follows without exception *a more or less considerable swing back in the direction of a homodromous, i.e. positive, after-current corresponding with a passing or permanent diminution of negativity of the cathodic ends of fibres.* If the period of closure is protracted ever so little, the effect soon passes into its contrary, or at any rate becomes diphasic (positive,

with negative fore-swing). *There can be no doubt that the positive kathodic after-current is in this case produced by an inhibition (developed at the physiological kathode at break of the exciting current) of the existing persistent excitation, and consequent relative positivity of the points of fibres in question.*

As we have repeatedly had occasion to observe, the effects of the changes in the excited muscle-substance produced under the influence of the anode, during closure of the current, are analogous in every particular to those which are perceived under the same conditions at the kathode on opening the current. This is true, not merely in regard to change of form in the muscle (which in both cases may be identified as a localised relaxation), but also of the concomitant electromotive phenomena, characterised by relative positivity of the entrance, or exit, points of the current, by which a negative anodic, or positive kathodic, after-current is produced respectively. Since the method of investigating secondary electromotive phenomena only determines the consequences of electrical excitation after *opening* the polarising current, it is evident that—given the conditions necessary to the discharge of a visible break excitation, *e.g.* application of stronger currents and longer duration of closure—the positive anodic after-current which this produces will become prominent, while the negative after-current only appears occasionally as a fore-swing. Only in the case in which the appearance of the break excitation is in any way hindered or prevented can we expect to see marked effects in the direction of a negative anodic after-current, as, *e.g.*, in exhausted preparations, or after killing the anodic ends of fibres.

It is not therefore surprising that muscles which are *ab initio* in a state of persistent excitation (tonic contraction) should react to current, both as regards visible changes of form and galvanic after-effects, analogously with veratrinised muscle. It is clear that the phenomena of inhibition, which appear during closure at the anode, on opening at the kathode, in contracted cardiac, as well as in holothurian, muscle, must correspond with positivity of the points in question as against all others; in the adductor muscle of anodonta also (which is characterised by pronounced tonus), not only negative anodic, but also positive kathodic polarisation must from experimental data be reckoned among the regular consequences of the passage of the electrical current (71).

As regards preparations which are as far as possible free from tonus (relaxed), we find as a rule, as in striated muscle, on leading off from the kathodic end and middle of the muscle, that negative after-currents predominate; these, in consequence of the slow disappearance of the persistent closure contraction, are very protracted, and are always most pronounced when the conditions are most favourable to the closing excitation. On fresher and more tonic preparations, on the other hand, a positive kathodic after-current predominates; it either appears alone, or is introduced by a negative fore-swing. Like positive anodic, positive kathodic polarisation is found to be dependent upon the strength and duration of the exciting current, and increases, generally speaking, in ratio with it. There is, moreover, an alternation between the antagonistic effects of polarisation at the kathode precisely similar to that at the anode, since the negative after-current retreats into the background in proportion as the positive is stronger, and *vice versa*. As a rule, it is not difficult to find in any given case a strength of current and duration of closure, at which monophasic positive effects alone are visible on the side of the kathode. But even then repeated excitation with homodromous currents soon brings about a diphasic action, since the positive after-current becomes steadily weaker, with simultaneous increase of negative polarisation.

In regard to the anodic after-current there is almost perfect correspondence between monomeric striated, and smooth molluscan muscle, save that every effect, including the galvanometric consequences of excitation, makes its appearance at a much higher current intensity in the latter. As a rule the negative anodic polarisation of molluscan muscle increases with increase in current intensity, but only within a certain range, beyond which a rapidly increasing positive after-current appears, so that there is once more a diphasic effect with diminishing phase of negativity, terminating with a simple positive variation. This latter, in striated muscle, is essentially dependent upon the actual excitability of the preparation, *i.e.* appears earlier, at less strength of current and duration of closure, in proportion as the muscle is more excitable. With regard to all the characteristics of positive anodic polarisation—its dependence on the state of excitability of the preparation, strength and duration of closure of the exciting current, localisation at the anode, and greater permanence

—there can be no doubt that it must, as in striated muscle, be regarded solely as the expression of the opening excitation. This is also evident from the fact that in perfectly fresh and highly tonic preparations, positive anodic polarisation, like the persistent opening contraction, preponderates over the negative kathodic polarisation, or expression of the closing excitation (especially at the first stimulation); the development of the positive anodic after-current is also, as in striated muscle, delayed or prevented by killing the anodic end of the muscle.

This is not true of the positive kathodic after-current, which both in striated and smooth muscle is not merely not weakened, but even considerably augmented by killing the end of the muscle.

It is important to the theory of positive kathodic polarisation that, as Hering found, there is sometimes, even in the perfectly fresh sartorius of *R. esculenta*, and still more in *temporaria* (directly after the first excitation with the battery current), a weak deflection of the magnet in the direction of a positive kathodic after-current, which may even attain a considerable magnitude. A certain limit of closure is essential, as otherwise diphasic or simple negative effects are produced. After killing the end of the muscle corresponding with the physiological kathode, these effects are considerably augmented, and it is then for the most part, even on the less sensitive preparations, easy to produce tolerably strong positive after-currents, on exciting with afterterminal (admortal) battery currents. They can thus be induced, as it were, artificially, by killing the kathodic end of the muscle. Since in this case the make excitation is entirely or partially excluded, we cannot, apart from other reasons, admit the interpretation recently attempted by Locke (17), who explains the positive kathodic after-current as the consequence of a persistent excitation which is longer sustained in the continuity (middle) of the muscle than at the kathodic end. We are convinced that the same effects appear when the sartorius preparation has *not* been previously treated with physiological salt solution, which, according to Locke, predisposes the muscle to tetanus contraction.

After due consideration of all these facts, and more especially of the striking coincidence between the conditions of the entrance and mode of manifestation of positive kathodic polarisation in the partially veratrinised muscle, on the one hand, and after killing

the kathodic ends of fibre in normal striated and smooth muscle in the other, we still believe our original interpretation to be the most probable, *i.e.* that here as there we are in face of a condition antagonistic to excitation, developed on breaking the exciting current at the physiological kathode, and a consequent relative positivity of the points at which current leaves the muscle to all other points in its continuity.

The local contraction often shows macroscopically, in all cases easily with the microscope, that after killing the ends of fibres at one end of a normal, regularly constructed muscle, the immediately adjacent excitable sections of the same are in a condition of more or less pronounced continuous excitation.

From this point of view, however, there is nothing remarkable in the appearance of positive kathodic after-currents; they are much rather the immediate and necessary consequence of every such injury, on the presumption of a kathodic opening inhibition. Such a preparation exhibits no essential difference in its reaction from that of a muscle treated locally with veratrin immediately after a momentary stimulus.

The last question to be discussed is how we are to conceive of positive kathodic polarisation in the normally uninjured, currentless muscle. Locke's theory (*l.c.*), which refers it to a surplus of excitation near the centre of muscles treated with NaCl, has already been considered. We regard it as answered by identical experiments on perfectly fresh, non-moistened preparations.

The positive kathodic after-current which then appears under certain conditions, cannot be forthwith compared with the corresponding effect in the uninjured molluscan muscle; for in the last case we have a tissue which is in every part in a state of continuous (tonic) excitation, while in normal striated muscle this is not so. If in the first we find only the consequences of a quelling of the tonic excitation, appearing at definite points, and a consequent *relative* positivity of those points, in the second we are forced to take into account a local alteration of the "resting" muscle-substance, as exhibited in the given instance by a positivity of the same towards other unaltered points of fibres. As we see at once, such a change at the kathode can, under the obtaining conditions, be regarded only as the consequence of the previous make excitation, through which the same points of fibres undoubtedly become strongly negative; so that we are forced into

the conclusion that there is here, as it were, a reaction of the living substance towards the preceding excitation.

The results arrived at in the previous discussion of the visible effects of electrical excitation in cardiac muscle, as also in different smooth muscular parts (holothurian and echinus muscle), are essentially confirmed and elucidated by these secondary electromotive phenomena. For they establish with certainty the general validity of those conclusions to which (more particularly) the observations on the effects of excitation on cardiac muscle in a state of alternating contraction had pointed.

The theory of two inhibitory processes antagonistic to the polar processes of excitation, which we found to be inevitable *re* cardiac muscle in systole, now proves to be the simplest explanation of the consequences of electrical excitation of striated skeletal muscle. This is equally true of the mechanical effects of excitation, and of the electromotive after-effects. The two methods of investigation, whether by testing the changes of form in the excited muscle, or by ascertaining the state of polarisation at the end of excitation, complete themselves reciprocally, so that a satisfactory view of the nature of the changes due to current is first obtained from the combination of both methods. We must especially remark that a direct proof of the existence of an antagonistic process, following or preceding the excitation, as expressed in corresponding changes of form in the muscle, is obviously possible only during pre-existing persistent contraction, but may in other cases be concluded very indirectly, *e.g.* by examination of the alterations of excitability. On the other hand, the investigation of secondary electromotive phenomena gives positive evidence of the existence of polar antagonistic processes in the resting muscle also.

In conclusion, the positive anodic and negative cathodic after-current on the one hand, the positive cathodic and negative anodic after-current on the other, are due respectively to the antagonistic polar alterations of the muscle-substance, one of which tends to negativity, the other to positivity, of the points of fibres implicated. To the former correspond (as mechanical effects of excitation) the closing and opening contraction, to the latter (where this is a tonic state of contraction) the closing and opening relaxation. The one, like the other, is conditioned by chemical alterations in the excitable muscle-

substance, arising under the influence of current, as to the nature of which nothing definite can at present be predicated. But while the changes consequent upon closure of the current are directly engendered by the latter, the opening effects relate essentially to phenomena of reaction in the altered muscle-substance itself, and not merely the anodic opening excitation, but the kathodic opening inhibition also, must be interpreted in this sense.

CHAPTER V

ELECTROMOTIVE ACTION OF EPITHELIAL AND GLAND CELLS

EVEN in the muscle it is not possible to make any sharp separation between "current of rest" and "current of action," seeing that both manifestations are to a certain extent distinct in degree only, and still less can this be effected with regard to the electromotive action of other animal and plant cells, in which differences of potential (irrespective of whether they appear before or during artificial excitation, and are relatively altered in one or the other direction) are always and solely the expression of chemical dissimilarity in adjacent parts of the living *continuum*. From this point of view therefore it is purely arbitrary, and indeed illegitimate, to speak of the "rest current" of a glandular, mucous membrane, or vegetable cell-aggregate, in contradistinction to the current of action, since in both cases we have a reaction deriving from the same cause, *i.e.* the presence of certain chemical processes of metabolism at given points of the mass of protoplasm, which are only altered quantitatively or qualitatively, by direct or indirect excitation. This does not of course exclude the event that with initial absence of current in such parts, differences of potential may be first called out, as in "parelectronic" muscle, by excitation.

It is therefore advisable to treat the electromotive reactions of glandular and epithelial cells together, without separating the discussion of the effects which appear during rest and during action, as was convenient in muscle. It is perhaps a consequence of the difficulties which the long-prevailing molecular theory threw in the way of any systematic account of the facts under consideration, that the experimental treatment of this part of the field is quite disproportionate to

the development of muscle and nerve physics, although some fundamental researches date as far back as the discovery of the muscle current.

There was for long a certain disinclination to attribute electromotive activity to cells of which a regular molecular structure, comparable with that of muscle, could not be predicated. Engelmann (72) in 1872, during a discussion as to whether the electromotive action of the frog's skin should be referred to the glandular epithelium, expressed his reluctance "to assume in cells which, like those before us, exhibit no sign of regular, axial arrangement of the particles, any regular, electromotive, structure capable of giving external visible response," and maintained that the gland-muscles were the sole effectual source of the electrical currents within the glandular layer.

As we have seen, du Bois-Reymond, whose name once more heads these investigations, was led by his attempts to demonstrate the supposed current of rest in uninjured muscles *in situ* through the skin, to the discovery of the marked electromotive activity of the frog's skin. On bringing any two points of the uninjured surface of a piece of excised skin, stretched on a glass plate, with leading-off pads of salt clay, into unequal contact, he always obtained a current which flowed within the skin from the pad last applied to the other. When both pads were applied as nearly as possible simultaneously, the needle remained at rest—comparatively speaking.

Du Bois-Reymond at once recognised that this effect was produced by the non-simultaneous contact. "Each point of contact is the seat of electromotive force in the direction of pad to skin, *i.e.* inwards; but the contact of the salt solution acts at the same time upon the cause of the electrical impulse. Hence, with dissimilar contact, there is a current in the direction of impulse from the last point of contact, which continues until the difference in impulse at the two points becomes negligible." Du Bois-Reymond next obtained much stronger deflections on leading off from the external and internal skin surface, always indeed in the direction from the former to the latter. Here, too, the impulse was soon abolished by salt solution, and was *ab initio* nil when the surface of the skin was painted with NaCl before leading off from it. The current was equally neutralised by scraping off the

epithelial and glandular layer. Since du Bois-Reymond found the skin current particularly strong in the toad, where the skin glands are vigorously developed, while the glandless skin of fishes (eel, tench, pike, perch) appeared entirely devoid of current, the presumption was "that the electromotive activity of the skin is in relation with the special dermic secretions peculiar to the naked amphibians." This view subsequently obtained substantial support from the observations of Rosenthal (75) and Röber (76). The former found not merely that the skin glands of the frog and other naked amphibians are the seat of electromotive forces, directed invariably from mouth to fundus, but that the same holds good of the mucous glands of the stomach, so that these electromotive forces "may with great probability be regarded as an essential property of glandular substance, just as we are accustomed to reckon electromotive forces among the essential vital manifestations of nerve and muscle."

This view is opposed to a later theory brought forward by Engelmann (72, p. 97), according to which the "gland currents" in question are of "myogenic" origin, initiated by the layer of contractile fibre-cells which surround each glandular body externally. Engelmann tried to make good this interpretation, which of course stands and falls with the pre-existence theory, from a long series of excellent observations, to which we shall frequently have occasion to return in the sequel. Yet it is incontestable that even from the standpoint of the pre-existence theory, the reaction of the skin current of the frog tells against rather than for Engelmann's hypothesis.

Hermann, again, proposes "that it is not, or not pre-eminently, the glands, but the *epithelial layer* which is (during rest) the seat of electromotive skin action." The reasons which originally compelled du Bois-Reymond to regard the glands as the essential cause of the skin currents in naked amphibia, *i.e.* absence of the same in the "non-glandular" skin of fishes, were believed by Hermann to be put out of court by the demonstration of a regular, ingoing skin current in a great number of the fishes examined (75). To this it might certainly be objected that the skin of the fish is not really glandless, but contains innumerable unicellular mucous glands ("goblet cells"), which in many cases may be regarded as one large, superficially flattened, mucous gland

(cf. F. E. Schultze, 78). And since we know that neither morphologically, nor with regard to physiological function, is there any fundamental difference between uni- and multicellular mucous glands, it is natural to regard the rest current of the fish's skin as referable to the goblet cells which function as unicellular glands. Hermann actually does this when, in terms of the alteration theory, he reckons each partial mucin metamorphosis of single cells, as well as the elements of the secretory glands, as a source of regular electromotive action, a force "which, entering by the free epithelium, is directed in the gland from lumen to matrix." Such currents are, in fact, demonstrable wherever mucin-forming cells, or glands, are present (skin of fish and naked amphibia, tongue, mucous membrane of throat, stomach, and cloaca). And that electromotive action may further, in Hermann's sense, be predicated of other non-glandular epithelial cells seems to be established by the recent researches of E. Waymouth Reid (88).

Seeing that, with the exception of the plant currents to be considered later, the experimental data of "cell currents" are founded almost solely upon electromotive action in uni- and multicellular mucous glands, the details of these observations must be examined a little more closely. The most appropriate object for experiment is perhaps the tongue of the frog, with its wealth of goblet cells and mucous glands, in which, moreover, it is easy to expose the secretory nerves. As regards the opinion expressed by Engelmann (*supra*) of the origin of skin currents, it is notable that the lingual glands containing characteristic mucous cells lie free of muscle in the connective tissue immediately under the surface, the papillæ of which are covered with a single-layered epithelium consisting of goblet and ciliated cells. The mucous, viscous content of the glandular membrane is everywhere, as appears from transverse sections, in direct connection with the mucous layer covering the surface of the tongue, as we should expect from the wide mouth of the glands. The epithelium of the under surface of the tongue, turned to the floor of the mouth, is also rich in goblet cells.

Various methods may be employed to investigate the "current of rest" in the tongue, as will presently be described. Speaking generally, we may picture the surface of the tongue as a freely and irregularly folded surface, covered in its whole extent with a single layer of secretory cells, intermixed sparsely with ciliated

cells. The glands thus appear merely more or less deeply pitted in the continuity of the layer of cells, from the inner surface of which it is possible to lead off, since, as was said above, the secretory layer covering the tongue is nearly everywhere in direct connection with the fluid contents of the glandular membrane. If the tongue is excised at the root, and stretched upon any indifferent conducting surface, such as a block of salt clay, we shall obviously have to test the electromotive action of the epithelium of the whole upper surface (which clothes not only the glands but also the papillæ lying between them), even if the inferior surface of the tongue were not invested with a similarly constructed, even layer of cells, the single elements of which are generally placed symmetrically with those of the upper surface. Between the two lies a thick layer of connective tissue and striated muscle, which, under normal circumstances, must be regarded as non-electromotive.

In every case, therefore, it is possible to lead off from the basal part of the individual cell-elements of the upper and lower surface of the tongue. On the assumption of a perfectly equal electromotive action of the epithelium of both surfaces (a hypothesis which must, however, be excluded on account of the very different mass-relations of the cell layers in question), there would, of course, be no effect on leading off from two symmetrically opposed points of the upper and lower surface. The web of the frog's hind-leg, *e.g.*, on leading off from both sides, gives only weak and irregular electrical effects on account of its symmetrical structure. The tongue, on the contrary, under the same conditions, yields almost invariably a strong current directed in the leading-off circuit from under to upper surface, *i.e.* an "entering" current in Hermann's sense, which often sends the scale far out of the field of vision. Since, as will be gathered from the following, the lingual currents undergo very considerable alteration from the most insignificant mechanical impacts, it is essential to proceed with great caution, avoiding the slightest pull or contact. The following was, in our experiments, the most convenient method of leading off from the excised tongue, through which blood is no longer circulating. The frog was weakly curarised, until it just lost power of movement; the external skin was then carefully removed along the whole region of the lower jaw, to exclude any possible complication from its

electromotive action,—the jaw was exarticulated and divided by a sharp cut below the apex of the tongue. It is true that muscles are injured by this method, and that current may diffuse from their stumps into the galvanometer circuit; but the effect of this is practically negligible against the force of the lingual current, as shown by control experiments in the same preparation when the tongue has been removed. The lead-off is accomplished as follows: the lower jaw, with its under surface, is placed on a block of salt clay of corresponding proportions, which admits of a lead-off from the lower side of the tongue, by the floor of the mouth, when one brush-electrode is brought into contact with it, while the other is applied to any given point of the upper lingual surface. It should be noticed that the floor of the mouth on which the tongue is lying is itself invested with a mucosa rich in goblet cells, and therefore gives electromotive reaction. But if the tongue is cut out at the root, and the lead-off effected as before from the clay block and surface of the mucous membrane, which had previously been covered by the tongue, there will usually be very slight deflections only, in one or the other direction, so that the disturbance is negligible.

There can thus be no doubt that, however the lead-off from the tongue is effected, the results observed are produced respectively by the electromotive activity of the *surface epithelium* in its widest sense (epithelium of glands and papillæ), even if the absolute intensity of this latter is modified to a degree that cannot always be exactly determined, by the unavoidable inclusion, on leading off, of other electromotive elements. This is most clearly shown in the fact, that (in every experiment arranged as above) the current, which sometimes makes a very vigorous entrance, driving the scale far out of the field of vision, dwindles after destruction of the surface epithelium into irregular traces, though neither the epithelium of the under surface of the tongue, nor that of the floor of the mouth, can be perceptibly affected by it. On the other hand, it is easy to ascertain that even little scraps of mucosa, snipped out with a flat scissor-cut from the surface of the frog's tongue, and examined, after a short rest, on a bed of salt clay, are, just as much as the tongue, the seat of a strong ingoing current. Thus we may regard it as certain that the normal current of rest in the tongue is essentially due to the electromotive action of the surface epithelium, its glands included.

As regards the strength of the "rest current" under various conditions, a very brief observation of the object in question makes it plain that the electromotive reaction is far more dependent upon external accidents and internal changes than is the case with the muscle current. The individuality of the frog, its state of nutrition, temperature relations, the time of year, and other circumstances, affect the currents of the mucosa so strongly that the results are extremely variable.

On comparing the muscle current with that of the lingual mucosa, the most striking point is the great inconstancy of the latter, apparent in every kind of lead-off—most of all, however, by Hermann's method (*supra*) of leading off from the uninjured, weakly curarised frog at the upper surface of the tongue, and any indifferent portion of the body (from which the skin has been removed, but which is otherwise totally uninjured), such as the muscles of the thigh or leg. If, under these conditions, the entering "current of rest" is at all vigorous, the scale will hardly remain at rest for a moment after compensation, but swings in the direction of now increase, now decrease, of the existing current. These oscillations, which are sometimes merely indicated, may in other cases extend over many degrees of the scale, while during the observation the current of rest may take up a perfectly different mean. Sometimes the antagonistic deflections occur with a tolerably regular rhythm, but in most cases this is not recognisable. The possibility that the lingual glands may, as has been shown, be innervated from the central organ, suggests that the effects described may be due to a central excitatory impulse; the oscillations, however, also appear, though as a rule feebly, in the preparations of the lower jaw described above, so that in any case their immediate cause must be sought *in the tongue itself*.

If the lingual rest current is led off as above from the whole uninjured frog, the lower jaw being drawn back as far as possible by means of a thread passed through close to the tongue, while the animal lies on its back, the current, immediately after applying the electrodes, is almost invariably found to be rapidly increasing, and it may happen that a current which is extremely weak when the throat is first opened, will drive the scale out of the field a few minutes later. On taking off and replacing the electrode in contact with the surface of the tongue, at the same or any other

point, a regular diminution may be observed, with subsequent increase of current. The explanation of these effects can only be given in connection with other facts to be communicated later.

The marked effect produced by *changes of temperature* upon the electromotive action of the frog's tongue claim fuller discussion. If a curarised frog is kept for a long period (several hours) at a low temperature, the tongue, if examined as quickly as possible, will often exhibit a reversed, *i.e. outgoing* current of rest, which is frequently no less strong than the previous normal incoming current. As a rule, this reversed current diminishes pretty quickly as the preparation gets warmer. A short stage occurs when, under the given conditions of leading off (surface of tongue and exposed muscles of leg), no difference of potential is visible, after which the normal entering current gradually develops. The strongest reversed effects are obtained when weakly curarised frogs are packed in snow for some hours. If the lingual current is then investigated as above in the uninjured animal as quickly as possible, before any heat effect becomes visible, an extraordinarily strong deflection, far exceeding the scale, may often be seen in the direction of an outgoing current. And if such a "cold frog" is left in a warm room, the normal entering current will develop, as has been shown, more or less quickly. These experiments led to the further testing of heat and cold upon the excised tongue, using throughout the preparation from the lower jaw. Since 0.5 % NaCl solution was found to be tolerably indifferent for electromotive action of the tongue, immersion for hours in this fluid producing no noticeable effect, the simplest method of warming or cooling appeared to be to place the preparation in solutions of the same molecular strength at different temperatures. And this showed, without exception, that every preparation that had previously acted strongly in the normal direction now became currentless in the shortest possible interval, developing indeed in most cases a reversed (outgoing) current, provided it were placed on snow in a watch-glass filled with physiological salt solution, and covered with a bell-glass for some hours at low temperature (0–2° C.) The same result is also obtained if the preparation on the clay block is simply placed for several hours in a moist chamber in a cold, but not frosty, room (at about 2–4° C.) In every case the outgoing current of rest can be reversed almost instantaneously if the

preparation is immersed in physiological salt solution at about 20–30° C. These experiments involuntarily recall Matteucci's statement of the effect of cooling upon the muscle current. Without denying this, we must however point out the enormous difference in degree which is apparent in either direction, in the two cases. The "rest current" of the muscle (*i.e.* the demarcation current of Hermann) is certainly weakened by intense cooling, but is never abolished, much less reversed in direction.

We have found that preparations of the tongue, which, when *freshly* examined, exhibit strong electromotive action in the normal direction, afford reversed currents less readily on cooling than those whose activity, from long immersion at a not unduly high temperature, is already considerably diminished. Thus we found throughout that the frogs best suited to these experiments had in every case been kept for a long time during the winter in a warm room. "Cold frogs" nearly always afforded preparations, which if freshly examined gave very strong and comparatively constant currents, opposing, as it were, a greater resistance to the influence of cooling than the equally strong, or even stronger, rest currents of "warm frogs." With this may perhaps be connected the fact that spring frogs packed in snow usually yield a much stronger outgoing lingual current than winter frogs. The latter, however, according to our experiences, may be easily thrown into a similarly favourable disposition, if they are kept for two or three days before the experiment in a warm room near the stove. Then on leading off the tongue current the deflection obtained will often be as marked, in the same direction, as in cold frogs, only it is, so to speak, in labile equilibrium. On cooling, it gives way much more quickly to the opposite current than in fresh, cold frogs, where it is sometimes quite impossible to abolish the normal entering current by the methods of cooling described so far.

This does, however, occur without exception, if melting snow or ice is brought into direct contact with the surface of the mucosa, and we have never met with a case in which, under such conditions, there was not a real reversal of the normal rest current. In detail, however, the reaction in different preparations varies considerably in its proportions, wherein the effect of the conditions already cited is once more evident. We have found it most convenient to introduce small, even plates of ice—not too thick

(as may easily be obtained by freezing thin layers of water)—as carefully as possible between the tongue and the leading-off electrode. The current will then sink almost instantaneously to zero, and is, as a rule, reversed in a few seconds. The new outgoing current may sometimes be of such dimensions that the scale flies out of the field. If the single application of ice is not sufficient, repetition of the treatment is sure to be successful. After the ice has melted, the reversed current generally diminishes rapidly, and finally turns round again as an entering current. The diminution, which occurs more rapidly at first than later, is not always uniform, but takes place with more or less considerable oscillations.

If the facts previously communicated are decidedly in favour of the view that we here have mainly an effect of cooling, the obvious objection must be answered that contact of the electrode with the melting ice might give rise to a "thermo-current." This conjecture is the more probable, since currents are actually known to exist in consequence of the unequal warmth of the leading-off, unpolarisable electrodes. Not merely are important thermo-electric effects caused by unequal temperature in the two tubes containing the glass-rods, but—as found by Worm-Müller and verified by Griitzner—a weaker "thermo-current," reversed in direction, may also arise between the clay plug saturated with NaCl solution, and the solution of zinc sulphate. It passes from zinc sulphate to clay, with an E.M.F. of 0.002 Dan. at 35° difference of temperature. Control experiments, effected for the most part with the clay block alone, as well as with dead, electrically ineffective preparations of the tongue placed upon it, gave only weak deflections in the same direction as before the experiments in question, *i.e.* the cooled electrodes were, so to speak, weakly positive. There is not, however, the smallest reason to refer the very marked action of normal preparations to this cause. Apart from all the other reasons that have been given, it is only necessary to point out that the full effect of the outgoing current appears also in the case in which the brush-electrode is first brought into contact with the tongue some time after it has been laid upon ice (after removing the water of liquefaction), when a marked deflection at once follows in the expected direction, and finally drives the scale off the field—which can hardly, in this case, correspond with any difference in temperature. Moreover,

in preparations of the lower jaw, which by alternate freezing and thawing had been rendered perfectly currentless, and had lain for some time in salt solution warmed to the temperature of the room, even repeated application of snow or ice leaves hardly any trace of an outgoing current.

From these observations we may take it as proved that the regular entering current of the mucous membrane of the frog's tongue is not merely diminished to zero with extreme rapidity when sufficiently cooled, but may also be reversed—when the reversed current, under some conditions, reaches the same proportions as those of the original “normal” current.

In the experiments last quoted, the surface of the lingual mucosa was moistened with the water of the melting ice, so that it became necessary to consider whether the results of the experiment were not due, at least in part, to this factor. That it was certainly not the main cause is amply proved by the facts above stated, but the strikingly rapid reversal of the current, as well as its E.M.F., might be partially due to a water effect. We accordingly examined the effect of the varying bulk of water on the electromotive properties of the lingual mucosa during “rest.” Engelmann (72) had already made an excellent series of observations with the same object on the skin of the frog, to which we shall return later. These relate to the action of water, and of different concentrations of salt solution, upon the equally ingoing current of rest in the skin. Since, as we shall find, there is in every respect almost complete agreement between the electromotive action of the external skin, and the tongue, of the frog, it might be assumed *a priori* that the same would be the case with regard to the effects of addition and subtraction of water. Owing to the extraordinary sensitivity of the lingual mucosa (*infra*) to the slightest mechanical stimulus, the fluid to be tested must not simply be poured on, or applied with the brush (which would easily lead to the worst fallacies), but the preparation must be dipped into watch-glasses containing the required solutions. After a shorter or longer bath, the lingual current is tested again, as described above, by leading off from a clay bed and the surface of the mucosa. While normal 0.6 % NaCl solution is indifferent for the tongue also, in so far that the power of giving electromotive reaction will persist for hours and even days if the temperature is not too high, the E.M.F. of the ingoing

mucosa current is always considerably increased if—after the deflection has been rendered approximately constant by long immersion in ordinary physiological saline—a semi-normal (*i.e.* 0.2–0.3 %) NaCl solution is applied: still more so if spring water or distilled water is employed.

A single drop of distilled water applied with the leading-off electrode to the surface of a tongue previously treated with physiological salt solution is sufficient to produce a strong *positive* variation of the mucous current, although the resistance in the circuit of course increases considerably. Even long immersion in spring water not merely fails to weaken the normal current, but may even maintain it at a permanently greater E.M.F. than 0.6 % salt solution. It is therefore out of the question that the antagonistic effects above quoted should be due to the action of the water of liquefaction, when the mucosa is cooled by the application of snow or ice. Such solutions as contain salt enough to cause dehydration, to a greater or less degree, of the tissues in contact with them, produce a reverse effect from water or highly dilute salt solution. With such we always find (*e.g.* with 0.8–1.5 % NaCl solution) a comparatively rapid fall of E.M.F. in the ingoing tongue current, which, between certain limits, rises again with equal rapidity when water is added.

It is very remarkable that in this case also, as on energetic cooling of the tongue, there may be a true reversal of the normal ingoing current, although the strength of the opposite current is generally far behind that produced by the action of cooling. It is possible in the same preparation, by alternate immersion in 1 % and 2 % salt solution, to give a successively incoming and outgoing direction to the current many times over. As a rule, a few minutes are sufficient to initiate these changes. Engelmann had already found in the frog's skin that very low differences in concentration of the salt solutions produced extraordinary alterations in electromotive response, from which we may conclude a singular sensibility of the active elements concerned, with regard to changes in the water content. It is well known that even while the frog's tissues are living, water may be drawn out of them vigorously by injecting strong solutions of common salt or glycerin at the back of the head. Half a cc. of the latter injected into the dorsal lymph-sac of a curarised frog is sufficient in a short time (1–2 hours) to draw

off so much water from the watery tissues of the tongue, that they appear visibly shrunken and darker in colour than under normal conditions. In this state the entering current of the mucosa is always very weak or wholly wanting.

These last appearances lead directly to the consideration of the mode of action of other substances which produce chemical metabolism in the living cell. In the first place there are the two gases which play such an important part in the vital processes of the organism, oxygen and carbon dioxide, whose special significance for certain electromotive reactions of plants and animals is well established. Engelmann showed that on driving out oxygen by an indifferent gas (N or H) the E.M.F. of the skin current sinks gradually, increasing again quickly so soon as atmospheric air is reintroduced, until the initial height is not only reached, but even exceeded. CO_2 on the other hand, produces an extremely rapid fall of E.M.F., which is only arrested when the surrounding atmosphere contains a low percentage of the gas. A similar effect of want of O has been recently demonstrated in plant currents by Haacke (*Flora*, 1892, Heft iv.) We can attest a similar effect of these two gases upon the frog's tongue. The method of experiment was essentially based upon that of Engelmann; the preparation (lower jaw and tongue lying on a block of salt clay) was placed with the leading-off electrodes in a gas-chamber, consisting of a glass vessel, with four tubes, through which the gases could be led into the chamber. The E.M.F. of the incoming lingual current invariably fell on driving out O, as well as on introducing CO_2 , in the first case rather slowly, in the second, on the contrary, very rapidly. This simple contrivance may also be employed for testing *anæsthetics* (ether, chloroform): even a small quantity of these substances in the form of vapour produces a considerable diminution of E.M.F. in the entering current, which, if the action does not last too long, is restored by driving pure air through the chamber.

The mucosa of the throat and cloaca of the frog give precisely similar relations. Engelmann (77) had previously demonstrated electromotive effects in both these preparations. Again, in both cases, we have, under normal conditions, an "entering" current, often of considerable E.M.F., and hardly below that of the lingual current. Yet the histological structure is widely different. Both

in throat and cloaca the mucous coat is "glandless" in the ordinary acceptance of the word, there being in both cases only a single layer of cylindrical epithelium, consisting in the throat of ciliated cells with goblet cells interspersed between them, in the cloaca almost exclusively of the latter. Multicellular glands are entirely wanting. From these very reasons the preparations afford much more obvious and simple conditions of leading-off than the lingual mucosa, so that certain objections to which the latter is fairly liable drop out of court without prejudice. Since in the cloacal mucosa ciliated cells are altogether wanting, while its electromotive action corresponds in every respect, on the one hand with that of the ciliated mucosa of the throat, on the other with the sparsely ciliated lingual mucosa, we cannot but conclude that in all three cases *the true electromotive elements are the mucous cells, whether present as elements of compound glands, or as goblet cells*. But it was necessary to test this view, inasmuch as Engelmann held the ciliated cells themselves to be the active electromotive elements, and was inclined to derive the throat current from them. Hermann, too, indicated as a possibility that the ciliary movement might be regarded "from the point of view of an ('irritative') alteration occurring in the external cell-layers." Our own observations do not, however, bear out this suggestion.

The method of investigation both in throat and cloaca was extremely simple. Engelmann, as a rule, separated out the mucosa from the layers beneath it, and led off from the inner and outer surfaces of the membrane stretched over a cork. But even with the greatest precautions this entails some mechanical injury, and since—as we have frequently experienced—the intensity of electromotive action in the mucosa is affected to an extraordinary degree by even the slightest stretching or tearing, it is preferable to lead off from the mucosa *in situ*. For this it is only necessary to remove the outer skin of the head as far as the wall of the upper jaw, so as to avoid any accidental interference from its electromotive properties, and then to cut out the whole upper jaw by as deep a section as possible. This is placed in a watch-glass in a little 0.5 % salt solution, with the mucous surface uppermost, after which it is only necessary to dip one brush-electrode into the latter, while the point of the other is in contact with any point of the mucous surface, in order to lead off with as little disturbance as possible.

Under these conditions the entering current is much stronger than in the separated membrane, and the only doubt can be whether electromotive action of other parts (injured muscles, etc.) may not be involved in it. Such interference can easily be excluded if the same preparation is examined, as before, after destruction of the surface epithelium, or the entire removal of the ciliated mucosa. We have never then observed any marked differences of potential, so that this objection must be regarded as unfounded. The mucous coat of the cloaca is usually examined by slitting the cloaca longitudinally as cautiously as possible, and spreading it out on a clay block without actually touching the mucous surface, which can then be led off as usual.

Up to a certain point the mere look of the membrane will show in the one case, as in the other, whether it will yield a strong or weak current. If the mucosa of the throat (as is usual in winter) looks transparently pink and moist, and if the cloaca is filled with soft or liquid matter, a strong current may be reckoned on with tolerable certainty; but if, on the contrary (as is usual in summer with frogs that have been in hand a long time), the ciliated mucosa is dim and pale, or the cloaca contains only a few hard excreta, the entering current, although generally present, will be extremely feeble. This seems a direct indication that the secretory activity stands in both cases in immediate and close relation to the electromotive action of the mucous membrane. To this it must be added that the ciliary movement often occurs normally, as far as may be judged from the onward movement of blood platelets or similar bodies, while the entering current is quite, or almost, wanting; and we have, on the other hand, though more rarely, observed cases in which, notwithstanding a weak ciliary motion, the E.M.F. of the current was unusually high. The mucosa in this case was invariably covered with a tolerably thick layer of slimy secretion. It would appear that the mechanical injuries associated with exposure and extension have a much less pernicious effect upon the ciliary movements of the mucosa of the throat than upon its electromotive action. We have frequently observed in these preparations that the ciliary motion continues for hours with the utmost vivacity, while minimal deflections alone indicate the presence of a weak entering current. The effects of pilocarpin poisoning may also be quoted in favour of the view here advanced, which regards

the entering "rest current" of the throat mucosa as a "secretion current." The lingual current is usually found at a certain stage of pilocarpin poisoning (two hours after injection of 1 cc. of 2 % solution of pilocarp. muriat.) to be extremely vigorous, and the same is true, according to our experiences, of the throat and cloacal currents. The deflection is normally so strong that the scale flies off the field.

Since there appears from the above experiments to be no proportion between vigour of ciliary movements and intensity of electromotive action, while the observations of Engelmann, which seem to indicate such a relation, are capable of quite another interpretation, we have so far failed to discover any reason why the entering current of the mucosa should be referred to any other cause than the homodromous lingual or cloacal currents, unless in the sequel there proves to be similar electromotive action on the part of a membranc consisting only of ciliated cells. We have seen that the uniformity of electromotive reaction in the two preparations in question, and the lingual mucosa, is almost perfect. This is true not only of the inconstancy of the current, but also of the effects of cooling and excitation. In nearly every case in which the E.M.F. has reached a certain height, oscillations of the magnet may be observed, from which we may conclude the presence of heterodromous forces, the sum of which corresponds with the momentary deflection. And just as this magnitude alters with time at one and the same point, it may vary at different points of the mucosa at the same moment. As a rule the entering current of the cloacal mucosa is far more vigorous than that of the throat—as might be expected *a priori* if the unicellular glands (goblet cells) are to be held responsible for it.

Engelmann had observed that this current is weakened by cooling, but it escaped his notice that under uniform conditions a total reversal may be possible. In fact, nothing is easier than to convince oneself that by laying a preparation of the upper jaw in 0.5 % NaCl solution cooled to zero, the strongest entering current may be made to disappear in the shortest possible time (5–10 minutes). Immersion in warmed salt solution (about 25–30° C.) calls back the normal current almost instantaneously. In order to produce an "outgoing" current of any considerable proportions, it is, as a rule, necessary

to make use of melted snow or ice; it also depends conspicuously upon certain conditions in the mucosa, which again are due to environment during the life of the frog. In the throat, as in the tongue, the best and most convincing results are obtained when the preparation is taken from a warm frog, and the original entering current not too pronounced. Accordingly the frogs (*R. temporaria*, not curarised) intended for this experiment were usually left two to three days in a warm room near the stove. In order, as far as possible, to avoid mechanical excitation of the mucosa by friction or pressure, it was found best to apply loose melting snow, a lump of which was placed upon the mucosa of the skinned upper jaw, and several times renewed before the current of rest was tested. The water of liquefaction is carefully removed with a brush, and the leading-off electrodes arranged in such a way that they are divided by a not too thick layer of melting snow from the mucous surface below them. Immediately after reading the scale the galvanometer is opened again by removing the electrodes from the mucosa, so as to avoid the development of accidental "thermo-currents" as far as possible. Exactly the same method is employed to investigate the effect of cold upon the cloacal current. In the one case, as in the other, a very rapid fall of the original E.M.F. is visible, accompanied, generally speaking, by reversal of the current, upon which it often reaches such proportions that the spot flies off the scale. When the snow is entirely melted the original E.M.F. of the current usually comes back in consequence of the increasing temperature. The experiment may be repeated many times on the same preparation with identical results.

We cannot doubt that the cooling of the surface epithelium here, as in the tongue, leads *per se* to the appearance of heterodromous electromotive force.

The skin of the leech is another no less favourable object for the study of electromotive action in superficially flattened, unicellular, mucous glands. After removing the connective tissue it is easy to free the skin with scissors from all ragged ends of tissue, so that only the cuticular muscle-layer is left. Then, on leading off from external and internal surface, there is invariably a strong entering current, which reacts under different conditions as described above.

The well-known homodromous electromotive action of the

skin in lower vertebrates (amphibia and fishes) must be referred essentially to the same causes as in the organs previously described.

By far the most thorough investigations relate to the electromotive action of the external skin of the frog, and we are more especially indebted to Engelmann (72) for a series of excellent observations, the value of which is in no way lessened by the incorrect interpretation he puts upon them. More recently, starting from certain theoretical considerations given above, Hermann has again made the skin of the fish the object of investigation, with results that are conclusive as regards his interpretation of the frog's skin-current.

Since the skin of certain fishes is, in those points which seem most essential to electromotive activity, precisely similar in construction to the objects last under discussion, a few observations upon it may be quoted. From the researches of F. E. Schultze (78), it has long been known that there is a varying mass of unicellular mucous glands, in the form of goblet cells, in the cuticle of many fishes, which in some cases compose the whole of the epithelium (*Cobitis*). The individual elements often reach a considerable size, and yield a mucous secretion, which makes the upper skin smooth and slimy. As always, the protoplasmic, nucleated portion of the cell is basal, *i.e.* directed towards the cutis, while the upper portion engaged in transforming the mucin opens directly upon the free surface of the upper skin. At the present time there cannot be the slightest doubt as to the secretory function of these cells, since the process may actually be watched under the microscope. Hermann, in particular, has contributed valuable data *re* electromotive activity of the skin of fishes. As compared with frogs, fish are less suitable objects, inasmuch as their upper skin is not, as in the frog, separated by great lymph spaces from the muscle, but grows into it. In many, and indeed most cases therefore, it is only possible to test the P.D. between a corroded point of skin (*i.e.* incapable of electromotive action) and one that is normal, when there will usually be a strong current in the same direction as in the frog's skin and mucous membranes (*supra*) under corresponding conditions, *i.e.* the corroded point of the skin is "energetically positive to non-corroded points."

We must, with Hermann, conclude from this fact "that the

skin of the fish, or, more correctly, every spot on the superficies of the fish, is, in exactly the same way as the skin of the frog, the seat of an electromotive force directed from without inwards, and very easily disturbed by corrosion." In the eel it is not difficult to strip off the entire skin, or to prepare pieces of it, but it is advisable in all cases that the fish under examination should be as fresh and uninjured as possible, since the electromotive activity easily receives a permanent check from any slight injury. E. Waymouth Reid and Tolputt (83) have recently observed reversal of the current on fatigued animals.

Under normal conditions the rest current of the frog's skin agrees perfectly with that of the fish—save from its greater strength in most cases—although the histological structure of the two objects presents fundamental differences. Mucous cells are not, as with the fish, the chief constituents of the surface epithelium proper, but are confined almost exclusively to the multicellular skin glands; the epithelium, on the other hand, is composed almost exclusively of polyangular prickle and bristle cells, those next to the cutis being more cylindrical in shape, while towards the surface they get more and more flattened, and are eventually covered over with a single layer of flattened epithelium. Only a few solitary goblet cells, small and flask-shaped, are found in the epithelium, near the surface, and even these (according to F. E. Schultze) do not open upon it.

Engelmann's observations (as confirmed by the author) are the best authority in regard to the normal entering rest current of the frog's skin—which is mainly to be referred to the great number of skin glands present.

The dependence of E.M.F. in the skin current upon the bulk of water in the tissues is once more apparent. We can readily see that the current will become weaker, in proportion as the epidermis gets drier, since the resistance to conductivity increases enormously with the latter. Simple moistening with water or dilute salt solution produces a rapid and considerable increase of E.M.F. in each such case. The greatest remainder of E.M.F. is obtained with pure water. "If a drop of salt solution of 0.2 % is applied, after washing with water has brought the E.M.F. to a constant height, it begins to decrease after a few minutes. Repeated dropping of the same solution depresses it still further, until it reaches a constant level. A

prolonged water-bath finally raises the E.M.F., in many cases, to the same height as before the application of the salt solution" (Engelmann). Stronger solutions of salt (0.4 – 0.8 %) act still more strongly and energetically. These experiments on the extraordinary effect of even very slight changes of concentration upon the magnitude of E.M.F. in the skin current cannot obviously be referred to changes of conductivity, but undoubtedly depend upon variations in the electromotive functions of the active cells, which go hand in hand with changes in bulk of water in the same. The skin of the frog is less sensitive than that of the tongue to mechanical impacts (pressure, traction). Still, after severe traction Engelmann found (*l.c.*) that the E.M.F. fell in a few seconds from 0.1 Dan. to 0.006 Dan. Protracted cold caused greater or less diminution of the entering normal rest current, without, however, reversing it. At a temperature of + 4° C. Engelmann still observed an E.M.F. of 0.08 Dan. Negative variations as a rule correspond with sudden positive heat variations, their duration and magnitude growing with increasing magnitude, duration, and spatial extension of the rise of temperature. Among chemical agents CO₂ is emphatically a substance, the effect of which is to diminish the force of the skin current "with extraordinary rapidity." In the space of the first half minute Engelmann has often seen it fall to a sixth, and less, of the original height. If the poisonous gas is removed soon enough (by blowing in air or hydrogen) the E.M.F. may return to its original proportions. So too, though in different degrees, the action of anæsthetics like chloroform and ether, which also produce marked negative variations even in minimum doses.

Want of oxygen, too, weakens the skin current after a long period, and may, after 1 – 2 hours, reduce it to zero. With renewal of air the E.M.F. increases more rapidly than it had previously diminished, provided that oxygen had not been drawn off for too long a period.

The great variability of skin and mucosa currents, and their extreme dependence on the most varying external influences, lead us *a priori* to anticipate that the effects of artificial excitation (whether direct or from the nerve) would, according to circumstances, differ very considerably. Here again the frog's tongue affords by far the most favourable conditions for experi-

ment, since the nerves that supply its glands can be exposed without difficulty.

We have seen the extent to which the strength of the normal entering "tongue current" is affected by the least disturbance to the surface of the mucosa. In nearly every case it increases rapidly after contact with the point of the leading-off electrode, both in the excised tongue and in the preparation *in situ*. That this is merely due to the decline of a negative variation (produced by contact of the mechanical stimulus) in the current of rest follows from the fact that, on closing the galvanometer circuit, the slightest movement of the electrode point on the surface of the tongue, or gentle rubbing of the spot led off, at once produces a rapid fall of E.M.F., which usually occurs the more vigorously in proportion with the strength of the maximal rest current. This negative variation declines very rapidly, and may often be reproduced if the excitation is repeated. Experiments to determine the magnitude of excitation required, show that extremely slight impacts are needed under favourable conditions. Stroking with the point of a hair, or the fall of a drop of salt solution, nearly always produces a marked variation. With stronger excitation distributed over a larger area, the effect is increased, and a current of rest that is not too strong may easily be reversed under these conditions, especially if (*e.g.* through moderate cooling) there is an *a priori* tendency in that direction. If kept at a low temperature in a little water, weakly curarised, *R. temporaria* will often exhibit a reversed (outgoing) rest current of considerable dimensions, if the leading-off electrodes are placed, one on the surface of the tongue, the other on the exposed muscles of the leg, directly after the lower jaw has been drawn back by a thread previously passed through it. This outgoing current, which must certainly be referred in part to cooling, is often as strong as the normal entering current, but diminishes rapidly if the electrodes are left undisturbed, and finally becomes reversed, *i.e.* normal. During the whole of this period the slightest friction with the tip of the electrode in contact with the tongue will at once produce a swing back of the magnet, in the direction of increase of the outgoing, or diminution of the incoming, current, followed again by a prompt reversal. In such cases the reversed current immediately after the throat has been opened is doubtless only partially due to the previous

cooling, and far more to the unavoidable mechanical excitation of the mucosa on freeing the tongue from the palate, to which it adheres in the natural position.

The normal entering current also declines considerably under similar conditions, and apparently from the same reason, and may even be abolished. If the same point of the lingual mucosa, which at first reacts strongly (in the direction of decline of negativity) when gently rubbed with the tip of the electrode, is repeatedly excited in the same way, the negative variation grows weaker at each excitation, and at last there will be no reaction; the normal current of rest is unaltered in strength, notwithstanding the excitation. The E.M.F. of the latter sometimes appears to increase considerably in consequence of temporary, local, mechanical excitation; but the method employed is hardly suited to the solution of this and other questions, and it is advisable to employ some stimulus that can be better graduated as regards intensity and duration. The electrical current in the form of the tetanising alternating currents of an induction coil is the best fitted for this purpose.

If the secondary coil is connected with two electrodes of platinum wire, which are then brought into contact, at a distance of 3 – 5 mm., with the moist surface of a block of salt clay (as used for testing the tongue current),—while the one brush electrode is in leading-off contact with the lateral surface, the other with the upper surface of the block, between the two platinum wires,—no trace of deflection will be detected in the galvanometer in the circuit, if the circuit of the secondary coil is closed by Wagner's vibrating hammer, and the coil not pushed home; but even in the latter case there are, as a rule, only very weak effects on the galvanometer, which in no way modify the consequences of excitation to be described hereafter. Before testing these on the living tongue, we ascertained of course by repeated experiments that the results described with the clay block underwent no alteration when a dead lingual preparation, incapable of yielding electromotive action, was placed upon it.

If, on the other hand, such excitation experiments are tried on normal tongue preparations—set up and led off as above—enormously marked effects may sometimes be seen, and almost exclusively in the direction of a negative variation of the rest current. Here again we see to a striking extent the dependence

of the magnitude of excitation effect upon the strength of the current of rest, as expressed both in the degree of deflection with a given intensity of excitation, and in the fact that it takes less strength of coil to produce a given deflection in proportion as the E.M.F. of the current of rest is lower. When the last is at a considerable height we have often, after compensating — with the coil at 160 (1 Dan. in the primary circuit)—observed a negative variation which drove the scale far off the field of vision. At the same time the changes of form and position in the tongue in consequence of direct muscular excitation were so insignificant as to exclude the possibility that the effects described can be caused by, or along with, them. Still it cannot be denied that these accessory effects, which are inevitable with strong currents, do produce a most undesirable complication, and we have therefore endeavoured to determine by special control experiments to what degree the excitation effects observed on the galvanometer are actually affected by them. It is not difficult to abolish the electromotive activity of the lingual mucosa, either locally at the lead-off, or on the entire surface, without affecting the deeper muscles, and with these the mobility of the tongue. If the appearance of the negative variation has been ascertained at any given position of the coil, and a grain of salt is then applied to the tip of the lingual electrode, there will follow immediately (partly in consequence of chemical excitation) a very rapid and marked diminution of force in the entering rest current. The excitation previously employed will now be ineffective, although the lingual muscles contract after as before stimulation. The same result is obtained on cautiously treating the mucosa with NH_3 in gas or solution. So that, while there can be no doubt that we have to include the *mechanical* excitation due to movements of the tongue contracting under the leading-off electrodes, it may, on the other hand, be accepted that the main result in this case is due to the *electrical* excitation of the mucosa. As a proof of this we may instance the behaviour of small fragments of the mucous coat, which are easily separated with scissors from the subjacent muscle-layer. As was said above, these, when examined on clay, as a rule exhibit before long a vigorous current, which on tetanising yields a strong negative variation without any material change of form in the fragment.

The behaviour of the cooled lingual mucosa, giving opposite electromotive action, is of interest; here, too, there is normally a negative variation, *i.e.* diminution of E.M.F. in the outgoing current, but this effect is generally much less, and therefore demands much stronger currents, than in the normal incoming rest currents. While this is the usual result with weak alternating currents, approximation of the coil under otherwise uniform conditions will often cause a positive variation after a first negative swing of greater or less amplitude, *i.e.* a temporary increase of the outgoing current occurring in the return process.

As regards, finally, the time-relations of the variation, these, with an entering current of rest, are highly characteristic. Without employing any finer artificial means, a latent period ("stage of latent electromotive action," Engelmann) may invariably be determined, its duration being essentially conditioned by the strength of excitation, in the sense that it decreases inversely with increasing strength of current. The deflection begins slowly at first, and rapidly attains its full value later; as a rule, the return swing of the magnet begins while the excitation is still in progress, and if the secondary circuit is left closed, runs in a zigzag course, sometimes interrupted by short backward movements in the direction of the negative variation. If, on the contrary, the excitation ends as soon as the deflection has reached its maximum, there will always be a rapid and uniform return swing of the magnet, during which the E.M.F. of the current not only regains its original proportions, but nearly always exceeds them to a marked extent, so that we are justified in saying that the negative variation further entails a weaker positive variation, which is relatively slower in its development, and still more in its decline.

If a sufficiently long interval is allowed between each pair of excitations, the experiments may be repeated with uniform results. Sometimes, however, the amplitude of the negative variation suddenly diminishes, and with each excitation there is a negative after-effect, which finally causes a permanent diminution of E.M.F. in the current. It is also important to avoid too rapid fatigue of the preparation, by an undue length of each individual excitation; protracted tetanus soon weakens the entering current permanently. We have already shown that the negative variation of the ingoing rest current is in a marked degree dependent on the strength of the latter, and diminishes very rapidly with the fall

of its E.M.F. This is best examined in preparations where normal electromotive activity has previously been altered in various degrees by treatment with dehydrating salt solutions. It is then found without exception that the negative variation is less on direct excitation of the lingual mucosa, in proportion with the weakness of the entering current. Soon, however, another phenomenon makes its appearance in the gradual development of a positive fore-swing and positive after-effect, which, as it were, enclose the negative variation. Sometimes the latter is wholly wanting, and even with strong excitation there will be only a monophasic, positive deflection, often of considerable dimensions. This only occurs, however, at a very advanced stage of dehydration.

Having in view the facts communicated above, which refer exclusively to the results of *direct* excitation of the lingual mucosa, we may curtail the discussion of the following, *i.e.* the appearances due to *indirect* excitation from the nerve, since in all essential points they coincide with the former. Hermann and Luchsinger (79), examining into the "secretion currents" of the frog's tongue when led off from two symmetrical points on the mucosa with excitation of the glossopharyngeal or hypoglossal nerve, express the "perfectly regular" result of their experiments as follows: "After a visible latent period, the excitation of a glossopharyngeal nerve produces a current in the excited mucosa, —ingoining at first, but which immediately gives way to an outgoing direction,—after which there is once more, whether the excitation is over or in progress, a powerful incoming current that long outlasts the excitation-(where this is not continued), reaching its maximum slowly, and then disappearing again with extreme reluctance." This effect will be seen to agree, generally speaking, with the results of *direct* excitation experiments, apart from the positive fore-swing and (in our observations far less strongly marked) positive after-effect of the second negative phase, which we have only observed, in the manner described by Hermann, in preparations where the normal electromotive activity is already considerably weakened. Our own experiments relate throughout to specimens of *R. temporaria* kept over winter during the months of January and February. We held it advisable with regard to the comparison possible between the series of experiments described above, and those to be discussed in the sequel, to continue leading off from the upper and lower surface of the tongue, with com-

pensation of the strong entering current which under these conditions is almost invariably present. The frog was usually slightly curarised—to the point of immobility—immediately before the experiment, since it seemed probable that the effects of excitation would be seriously weakened if the poisoning had occurred longer before, even if the circulation was normal, and the heart vigorously beating. In agreement with Hermann and Luchsinger, we found that the glossopharyngeal nerve acted like the hypoglossal, and there was at most a difference of degree in favour of the former. Since this is much more quickly and conveniently prepared, the following experiments are almost wholly based upon it. In normal, powerfully developed, entering rest currents, we invariably found as the effect of excitation of the nerve a monophasic, negative variation, the magnitude of which is dependent, as we have seen, on the force of the compensating current; this makes itself evident a short time (1–3 secs.) after the beginning of the excitation, and often reaches very considerable proportions. We never, however, observed reversal of a strong normal current in consequence of excitation. As a rule, after long protracted excitation of the nerve, the return swing of the magnet begins while it is still in progress, and oscillations are again to be observed frequently, the back swing being interrupted by renewed impacts in the direction of the negative variation. If the exciting circuit is opened at the moment when the magnet is on the point of turning, or a little earlier, the development of the original current follows more quickly than when the excitation is continuous; it is also evident that the backward phase of the negative variation follows regularly with increasing rapidity; and it is equally the rule that the original current of rest is strengthened by excitation, as was stated by Hermann. In our experiments, however, this positive “after-variation” was never stronger than, or even approximately as strong as, the preceding negative variation. Under normal conditions we have only seen this last introductory positive phase on a few occasions, and can therefore as little attribute to it, as to the positive after-variation, the significance attached to it by Hermann; according to our experiences the negative variation of the incoming current of rest has far more the appearance in every case of the undoubtedly characteristic effect of excitation, while the positive effect on the other hand

always retreats into the background. Yet this is by no means to say that the contrary might not occur under other conditions. The preceding statement refers only to lingual preparations which exhibit the normal reaction, *i.e.* vigorous entering mucosa current. It is also quite indifferent in what manner the lead-off is effected. In the entire uninjured frog we have either led off from the muscles of the leg and upper lingual surface, or made use of the previously described preparation of the lower jaw, which is easily brought into connection with the glossopharyngeal nerve, so that the experiments in question are directly comparable with the former. The last-named experiments made it possible to test the excitation of the nerve on preparations of the tongue in which the entering rest current has been weakened, or reversed, by treatment with strong (0.8–1.5 %) NaCl solution. As the nerve is not injured by a short application of solutions of this concentration, the excitation effects (manifestations) observed must principally be referred to the changes undoubtedly present in the glandular cells excited. In such cases we have frequently noted excitation effects which correspond throughout with those described by Hermann and Luchsinger, a strong positive effect being periodically interrupted by a weaker negative.

There is accordingly complete agreement in nearly every point of electromotive action between direct and indirect excitation of the lingual mucosa, another proof that in the methods of direct excitation employed we are only dealing with effects which originate in the mucosa. Another question, on the other hand, which cannot be answered as certainly, is whether in the previous instances direct and indirect excitation must not be regarded as identical, in so far as only the nerves which are situated in the mucosa are excited in the first case also. Some poison is required which, like curare in striated muscle, will entirely abolish nerve action without injuring the gland cells. *Atropin* at once suggests itself, as having long been known to abolish the effect of excitation in secretory nerves completely and permanently, in the most different glands. Hermann and Luchsinger showed that it had the same effect on the galvanic effects of excitation in the frog's tongue. Both after direct dropping on to the tongue, and subcutaneous injection, the strongest excitation of the nerve is ineffective, although, as we have repeatedly ascertained, direct excitation

of the mucosa after, as well as before, continues to produce a strong negative variation in the existing rest current. After large doses and longer poisoning we frequently found not merely that the incoming current of rest was considerably weakened, but that the results of direct electrical excitation were reduced in a marked degree. The conclusion is that atropin principally paralyses the *gland nerves*, without seriously injuring the cells.

It may be taken as proved that not only the glands of the external skin, but nearly all the glandular organs, are essentially affected by pilocarpin, as regards their state of activity, in the sense of a long-protracted, energetic excitation. Having ourselves (80) thoroughly investigated the action of pilocarpin poisoning upon the morphological behaviour of the lingual glands in the frog, it was the more interesting to determine the concomitant galvanic phenomena. In experiments many times repeated, in which the (non-curarised) frogs were injected with 1 cc. of 2 % solution of pilocarp. muriat. under the skin of the back, we invariably found two hours afterwards that the entering mucosa current of the tongue (which was covered with a visible layer of secretion) was developed with unusual vigour, and was often of considerable proportions. Corresponding with this, the negative variation, both with direct and indirect excitation, was extremely pronounced, and nothing has come under our notice so well calculated to exhibit the above-described normal reaction of the tongue in excessive proportion, as pilocarpin poisoning.

With regard to the action of this drug it was to be expected *a priori* that a long-protracted excitation of the secretory nerves would produce a similar effect. As in the salivary glands, so too in the mucous glands of the frog's tongue, it is possible by introducing a metronome into the circuit of the secondary coil to extend the excitation of the corresponding secretory nerves over several hours, without fear of too rapid exhaustion of the glands. Deep-seated histological changes ensue in both cases, which are in close relation with the secretory process (80).

If, during such rhythmical persistent excitation, the electro-motive phenomena are observed in the tongue (which should preferably be *in situ*, with intact circulation), there will be found without exception after a longer or shorter period—during which the initial current appears weakened in consequence of the pre-

dominance of the opposite current (negative variation)—a gradual, and, for the most part, irregular augmentation of the original ingoing current, which obviously corresponds with the positive after-effect of a short excitation, and may sometimes attain important dimensions. But the mucosa current, even after long-protracted excitation, will always continue to be directed inwards.

The mucosa of the throat and cloaca are of course capable of direct electrical or mechanical excitation also, and the effects are essentially the same as in the tongue, although these tissues are as a rule less sensitive. While, as we have seen above, the slightest contact with the lingual mucosa produces a negative variation of the normal entering current, which rapidly declines again as soon as the excitation is over, this is by no means usual in the throat or cloacal mucosa. In these a comparatively strong pressure, or pull, is required to produce any considerable depression of the "rest current," which subsequently proceeds as in the tongue. Much better results, and the only ones that are adapted to exact investigation, are yielded by local tetanising with the induction current. As regards the method employed, we may refer throughout to what has already been cited. In a preparation of the throat mucosa with very strong entering currents, excitation with gradual approximation of the coil produces even with weak currents (coil at 180) a distinct monophasic negative variation of the compensated rest current, which increases rapidly as the coil is pushed up, although even in the most favourable cases it does not go so far that—as is usual in the tongue under similar conditions—the scale flies off the field. A slight tremor at the beginning of the deflection sometimes betrays the existence of a heterodromous force, which, as we shall see, leads under other conditions to a *positive* variation. If the excitation is interrupted before the scale has come wholly to rest, the return swing of the magnet begins rapidly at first, and then travels more slowly to its zero, sometimes even beyond, in the sense of a reinforcement of the original current (positive after-effect). The manifestation of excitation is quite altered when the E.M.F. of the entering current of rest is lower. As in the tongue, only perhaps still more markedly, the strength of the negative variation depends upon the initial intensity of the normal, electromotive action of the mucosa. If this sinks below a certain limit, there appears regularly in

place of the monophasic, negative variation, a diphasic, and with very weak excitation, a monophasic, positive variation. The excitation effects are then dissimilar in detail, and to a certain extent very complicated. Generally speaking, it may be said that the positive variation preponderates the more, in proportion as the exciting, incoming mucosa current is *ab initio* weaker, while on the other hand the negative effects become more and more prominent with increasing strength of excitation, so that when the coil is pushed nearly home there will in the majority of cases be only, or at any rate chiefly, negative variation, the more or less delayed entrance of which often indicates the concealed presence of the opposite force. So too the rapid back swing of the magnet to its position of rest and even beyond it, as is often seen with lower excitation intensities; the primary, at first ingoing, negative variation always exceeds the subsequent positive swing in magnitude in such a case, as shown by the rapid reversal (when the exciting circuit is closed) of the magnet deflected towards the negative variation: from this there is but a step to the reaction in which the proportions of the two antagonistic deflections are inverted, the negative variation appearing only as a short prelude to the subsequent positive swing, which often under these conditions attains considerable amplitude, although the deflections caused by it never equal those of the stronger negative variation. Finally (with the lowest effective intensity of excitation), all direct expression of the negative variation may be wanting, a more or less definite retardation in the positive deflection being the sole indication of its presence. On cooled preparations, where the entering current was at zero, we have, even with the coil pushed home, obtained only simple, positive deflections (in the direction of the original E.M.F. of the current), and of no considerable strength. It is perfectly easy to remove the objection that the excitation effects described are caused by fallacies of any kind; it is only needful, as has already been described at length, to render the mucosa incapable of electromotive action, or to remove it entirely, in order to be certain that even on applying strong currents, excitation effects are totally wanting.

The non-ciliated cloacal mucosa and the skin of the leech react to electrical excitation readily like the ciliated throat mucosa. Here again, only perhaps in a still higher degree, the

influence of the initial force of the incoming current upon the excitation effects is apparent. The threshold of excitation actually lies, as a rule, much higher than in the throat mucosa. Before there is any definite effect in one or the other direction, there will often be an uneasy oscillation of the magnet, giving the impression that two antagonistic effects are in conflict. With weak currents the deflection of the positive variation finally preponderates, while with very closely approximated, or closed-up, coils, the contrary is the case without exception. A short, positive fore-swing is often to be seen, after which occurs the much stronger negative variation. At the end of the excitation the latter nearly always declines rapidly and completely. In several cases in which the entering rest current exhibited an unwonted intensity, there were, from the weakest effective currents to the strongest, only pure monophasic negative variations, which then attained proportions that are usually seen in the tongue only, under similar conditions. Thus, in one case, the cloacal mucosa of a non-curarised *R. temporaria*, stretched over a cork frame, and led off from both surfaces, exhibited an incoming current of such amplitude that the scale flew off; after compensation there was, even with the coil at 180, a distinct, negative variation of several degrees of the scale, and with the coil at 100 the scale vanished on excitation. Unlike the throat mucosa, the deflection, apart from small oscillations, remained tolerably constant so long as the excitation continued, after which it declined rapidly. Where the cloacal mucosa, as seems always to be the case if there is no fluid secretion, is currentless, or weakly active in an ingoing direction only, the strongest tetanising with the coil pushed home produces no visible negative variation; there is either no effect or at most a weak deflection in the sense of an ingoing current. This shows that the excitation effects depend upon the mucosa itself, and are not caused by the muscles lying beneath it.

In the richly glandular skin of Amphibia, the results of direct and indirect excitation are essentially similar. Engelmann (*l.c.* p. 136) carried out experiments in which pieces of skin (*R. temporaria*) were excited by single make or break shocks from an ordinary induction apparatus, the induction currents being led in by the leading-off electrodes. At the moment

of excitation the galvanometer was shut off, and it was ascertained that the induction currents had not left the electrodes perceptibly polarised. "Each excitation manifested itself by a sharp decline of *electromotive force*. This decline is not only relatively but absolutely greater, in proportion with the approximation of the coils, while at uniform distance of the coil it is much stronger at the break than at the make shock. After the first, second, and third excitation a positive variation (in a special case) follows the negative variation; the fourth excitation, however, weakens the E.M.F. permanently, to a considerable degree, and the last and most powerful break shock depresses it almost to zero, and leaves it weakened to about half the original." Our own observations agree in the main with these conclusions, when pieces of skin—from any part of the body indifferently—are stretched on a clay block, tetanised, and led off simultaneously with the excitation. If the frogs used (*temporaria*) have been kept in a cool room free from frost, in vessels with a little water, the electromotive action, *i.e.* entering current, will regularly and invariably be very powerful, with, as in the former cases, a corresponding monophasic negative variation, which appears even at a comparatively low strength of current, beginning after a latent period of 1–2 secs., and reaching its maximum value tolerably quickly; while as after-effect of the excitation a more or less considerable reinforcement of the original current of rest is usually visible, which declines slowly, and never approximates to the strength of the negative variation.

Direct electrical excitation of the skin of the eel's snout, which consists only of goblet cells, exhibits, according to Reid and Tolputt (83), a similar reaction to that of the frog's cloacal mucosa, *i.e.* with weak excitation and a low development of the rest current, there was a positive, with stronger excitation a negative, variation of the entering current, which was always very persistent. In the rest of the eel's skin there are, together with a less number of mucous cells, other kinds of secretory elements (club cells), which seem, as regards electromotive response, to give an opposite reaction. According to Reid and Tolputt (*l.c.*), there is, with a strongly developed ingoing current and strong excitation, a regular increase of the current (positive variation), while, conversely, weak excitation and low intensity of the existing E.M.F. seem to favour the appearance of a negative variation.

Our experiments show that the results obtained with indirect excitation of the frog's skin from the nerve agree almost exactly with those of direct excitation. Roeber (*l.c.* p. 3) employed a method by which he was enabled to experiment on the skin of the leg without much injury to it, and this is to be preferred to the preparation from the skin of the back used later on by Hermann. Under all conditions it involves much less injury to the skin, and, apart from the greater resistance of the preparation, makes it easier to test the effect of different reagents on the phenomena of excitation. We can either use Roeber's original method, in which, after setting up an ordinary "rheoscopic frog's leg," the skin "which covers the whole leg up to the knee-joint is divided by a circular cut at the ankle from the inferior portion, split up the anterior surface by a longitudinal cut, and then prepared and turned back from the entire limb almost to the knee-joint. The leg is then divided below the knee and taken off, leaving only the sciatic nerve, along with the knee-joint and skin of the leg." In order to lead off the skin current the prepared flap must be carefully spread out on a clay block, one electrode being in contact with this latter, the other with the centre of the exterior skin surface. Hermann's modification (75), as described above, is yet more convenient and sparing of injury; the whole frog is used, curarised to immobility, when the current can be led off with circulation intact—after freeing the pelvic portion of both sciatics (from the back)—either from symmetrical points of both skinned legs, or, as is perhaps better, from some point of the skin of the leg, and the exposed, undisturbed surface of the thigh muscles on the same side. In the latter case the whole skin current comes into play, and must, as a rule, be compensated beforehand.

In Roeber's experiment it was found that where the entering skin current was of any considerable proportions, excitation of the nerve invariably produced a greater or less diminution of E.M.F., and "as this occurs in a preponderating majority of cases," Roeber does not consider "this 'negative variation' of the gland current to be, generally speaking, the consequence of excitation of the gland nerves. With an originally low magnitude of current, on the contrary, there is sometimes increase instead of decrease, a positive instead of a negative variation." Engelmann also found in the same object an almost invariable

diminution of the skin current in consequence of nerve excitation, whether this were produced electrically, chemically, or mechanically. Even with the application of a single, vigorous, make induction shock to the peripheral stump of the sciatic, he observed a preliminary fall of E.M.F. to 25–30 %, which is naturally even more considerable with tetanising excitation. According to Engelmann, the course of an “elementary” variation in nerve excitation through a single momentary stimulus is as follows: “After a latent period, lasting with weak excitation for 4 secs., with stronger excitation for less than $\frac{1}{2}$ sec., the E.M.F. falls at first with increasing, and later with diminishing, rapidity—reaching its minimum after a few seconds with weak excitation, in 10–20 secs. with stronger stimuli; it rises again immediately, at first with increasing and subsequently with diminishing rapidity, eventually reaching its original proportions.” “But it does not often remain stationary at this point, especially when the skin has been resting for a long time before excitation. More frequently, during the next few minutes it rises higher in proportion with the strength of the previous excitation” (positive after-variation), “sinking down again slowly afterwards. If the excitation is repeated frequently, the positive after-variation fails to appear, and there will each time be a negative variation only. With prolonged tetanising excitation of the nerve, the depression of E.M.F. continues much longer, and outlasts the excitation. If the excitation is subsequently very vigorous, the positive after-variation may be wanting, even where it appeared unmistakably after a short excitation. The E.M.F. then remains permanently depressed, and renewed excitation only produces an insignificant diminution of it.”

Hermann (82), on the contrary, finds in the skin of the lower limb, and more particularly in the skin of the frog's back, in consequence of nerve excitation, either a *pure positive variation*, or the same preceded by a *negative fore-swing*, “which, however, is usually much weaker than the positive variation itself”—the latter being “the true main effect.” Hermann only found a pure negative variation twice in the skin of the back, and in the leg “in a negligible number of cases only” (three out of eighty frogs). The order of the deflection (in skin of back with tetanising excitation) is, according to Hermann, as follows: “At first the scale remains at rest for several (2–4) secs.; after this latent period

a tolerably rapid deflection (in the positive direction) is developed, but remains for the most part stationary, after which a slow further growth continues to the maximum. If the excitation is protracted, there will usually be reversal, and slow return; if interrupted at the height of its deflection, the scale will remain at the point of deflection for some time longer, or else continues its course a little further, returning then more slowly than the variation, to its original position." Hermann observed the same positive deflection after very short excitation: "At the end of such excitation the scale remains at rest for a certain time, and then pursues its deflection in the positive direction, though the variation is much less than with sustained excitation." Thus there is a complete antithesis between Hermann's results and the earlier conclusions, which is but little modified by the more frequent appearance of a "negative fore-swing" on the skin of the lower limb. Both Roeber and Engelmann have observed pure *positive* effects of excitation on the preparation last mentioned, although quite exceptionally and under conditions in which it is questionable whether the phenomenon is to be regarded as "normal." This was the case, *e.g.*, where the preparation, after being uncovered for some time in a moist chamber, exhibited "excessively weak" (entering) currents, and soon ceased to be excitable. Later on Bach and Oehler (81) found under Hermann's direction, in the first place, that the negative variation of the entering rest current of the skin was entirely dependent upon the strength of the latter (a fact to which we have frequently referred above), and on the other hand that in all cases where, whether through warming beyond a certain limit, or painting the skin with strong salt solution, the "current of rest" was perceptibly weakened, its negative variation declined rapidly, finally giving way to "an incoming secretion current," *i.e.* a positive variation. From this we may assume that in Hermann's experiments, frogs were used in which the skin current was very little developed. In the meantime he has made recent experiments (82), showing that in certain cases there is, even with a strongly developed, entering, rest current a mainly or exclusively *positive* variation, when the nerves of the skin are excited. This may be demonstrated on the skin of the leg in the tree frog, as well as on the skin of the salamander (*Proteus anguineus*).

If every diminution of the normal ingoing skin current is thus favourable to the appearance of homodromous (positive) excitation effects, it is *a priori* possible that even where the "current of rest" is altogether wanting, "an outgoing secretion current" may be present. In fact, Bach and Oehler showed that whereas after quite a short (6–8 secs.) action of saturated solution of sublimate the skin betrayed hardly any electrical activity, excitation from the nerve still produced tolerably pronounced effects, always in the direction of an entering current. We cannot agree with Hermann when he finds in this fact a convincing proof that the epithelial layer alone is intrinsically the seat of electromotive activity in the unexcited skin, only those effects which occur with nerve-excitation ("secretion currents") being true gland functions. For apart from the fact that even from the histological point of view this theory is highly improbable, it is also quite conceivable that in spite of the short duration of the sublimate bath, traces of the substance may penetrate into the gland cells, and reduce their normal electromotive activity, *i.e.* entering current, almost to zero, without abolishing it completely. We have, however, found ample proof in the preceding discussion, that under circumstances in which any kind of injury has weakened the entering current of the mucous secreting cells to a greater or less degree, homodromous effects may appear with direct or indirect excitation.

Since, as shown by Engelmann, the degree of moisture in the skin is far the most important factor in determining the strength of its normal electrical activity, as is also the case in true mucosæ, we should *a priori* presume that it would be possible, by altering the bulk of water, to alter the direction of the galvanic effects occurring when the skin is excited as in the foregoing. Indeed the experiments on the mucous coat of the tongue, throat, and cloaca, described above, points in this direction.

It is well known that frogs, when kept dry, gradually lose a large amount of water through the skin, but it would take a long time before they were sufficiently dehydrated by this method to be fit for experiment. This is effected much more quickly with the aid of *dehydrating substances*. A quantity of water can be drawn out of the frog's tissues in the shortest possible time by the simple injection of strong salt solution, or glycerin of sufficient density, under the skin of the back.

The two methods may be combined as follows. The frogs, when well dried, were placed in a large open glass, with a wire cover, the sides and bottom being wrapped in a clean, dry cloth. They were left thus in a warm chamber for at least 24 hours. They were next curarised as slightly as possible to produce immobility, and when paralysed, 1–2 cc. of 3–5 % salt solution, or better, 0.5–1 cc. glycerin, were injected into the dorsal lymph sac. After two, at most three, hours the dehydration is, as a rule, sufficiently advanced for the experiments to be started. It is unnecessary to enter into all the effects which can be observed on these frogs; they are sufficiently well known, and have no immediate connection with the facts before us.

If the electrical activity of the skin of such "dehydrated" frogs is tested as usual, either on single excised portions, or on the entire uninjured animal, the insignificant proportions, or almost complete absence, of the entering current is very striking. This is not merely due to the greater resistance of the dry skin, for the E.M.F. is slow to recover, even when the led-off parts of the skin are freely moistened with water or dilute salt solution. If an excised portion of the skin, no matter from what part of the body, is now excited directly, or if the freed sciatic is excited by leading off from the external surface of the skin of the leg, and the exposed surface of the muscles of the thigh on the same side, there will under all circumstances be an entering current, *i.e.* a positive variation of the current of rest, which either makes its appearance alone, or is introduced by a short negative fore-swing. Under these conditions there is never, as before, a monophasic negative effect. As regards the strength of the positive effect (always in the direction of an entering rest current), the right degree of dehydration is all-important, and there is a good deal of uncertainty in obtaining this. In favourable cases the positive variation may become as marked as was formerly the strongest negative variation. We have repeatedly seen deflections which drive the scale out of sight when the current of rest has been compensated. But if the latter is still considerable the positive variation grows less and less, and the negative fore-swing is correspondingly greater. Sometimes the entering skin current of the leg, immediately after freeing the sciatic nerve from the pelvis, is extraordinarily marked, notwithstanding the previous dehydration, and this is usually followed by a tolerably rapid

diminution during the experiment. It is not improbable that this is due to a (positive) after-effect of excitation of the nerve, produced by constriction. In such a case it is best to let the variation decline, and then excite electrically. In this way much more distinct positive variations are exhibited.

The order of the deflections produced by these latter is almost invariably such that after the expiry of the latent period and eventually of the negative fore-swing, the *positive* variation is rapidly initiated, and then becomes gradually slower, as if an antagonistic effect were asserting itself; sometimes it continues only for quite a short time, or even swings back a little, in the sense of a negative variation—finally, however, if the excitation is prolonged, the positive effect breaks through again, and the deflection becomes more characteristic. We are of opinion that this retardation in the course of the positive variation is actually to be referred to the opposite action of a simultaneously excited negative variation, so that, as always, the visible deflection is really the resultant of two antagonistic components. It is determined by the preponderance of one or the other of these forces.

To this we must also refer the fact that, at a certain stage of dehydration—which is safe to appear when the frog is dried simply by long detention in a dry chamber without water—the excitation of the sciatic, on leading off from the skin of the leg, which usually gives a strong ingoing current only, generally produces a distinct and fairly vigorous negative variation at the first excitation, followed by a weaker positive effect. On repeating the excitation at a later stage, no definite effect is usually apparent; but a slight swinging to and fro of the magnet, or oscillation at its zero, indicates an interference of antagonistic forces, which are nearly balanced. Under these conditions, a complicated variation may result from tetanising, which consists of four phases—an initial negative deflection, soon interrupted by an essentially stronger positive phase, which again swings back in a negative variation, and finally the magnet is again slowly reversed in the direction of a positive swing. The whole of this complicated process occurs during the excitation. The best way to observe the order of the separate phases is to take a frog at the stage of dehydration in which the skin of the leg still gives a marked ingoing current, and each excitation is accompanied

by a plain negative variation, followed by a weaker, positive swing—bleed it, and expose the nerves—letting it then lie in the chamber, and occasionally testing the effects of excitation; the ingoing skin current then declines gradually, the negative variation grows weaker, the positive effect stronger, and at last (after a brief interval of total failure of effect) it takes complete possession.

As Hermann pointed out, there is always a fairly protracted after-effect from the positive, in contradistinction to the negative, variation—the deflection increasing for some time after the excitation is over; the decline, too, follows more slowly than with the negative variation.

An interesting reaction appears in frogs (*temporaria*), fresh caught in the latter half of February. Any point of the skin at first gives a vigorous electrical variation, often far beyond the scale; excitation of the sciatic produces a corresponding and monophasic negative variation in the skin of the leg; this only declines very gradually and incompletely, so that a strong persistent diminution of the original current results, which again disappears almost entirely after a second short excitation. A third experiment is followed by a positive effect, preceded by a short, negative fore-swing. In another frog of the same group, the first excitation produced such a marked diminution of the original ingoing skin current that even at the second excitation the negative was replaced by a positive variation. Here we have proof of the extent to which the character of the variation is conditioned by the strength of the rest current. And we also learn from these experiments that Engelmann's attempted explanation of the *positive* effect is fallacious. He supposes that the positive increment produced by the free tension at the surface of the epidermis, in consequence of surface moisture from the skin glands emptied during excitation, over-compensates the negative effect originating in the decline of glandular energy.—This theory assumes that the surface cell-layers form a comparatively non-conducting layer in consequence of dehydration, "only a small fraction of the electrical tensions derived from glandular activity being apparent at its surface." Yet such could not be the case, either in the instances quoted above, or in the dehydrated frogs. For in the first case, no water had been drawn off, and the vigorous primary skin current shows that the glands were

ab initio concerned in its production. In the second, no trace of secretion even with the magnifying lens was to be discovered during excitation of the dry surface of the skin, which is so easy to detect under normal circumstances. The result remained the same when the skin surface was moistened with water, or 0.5 % salt solution. Hermann subsequently applied the same process of secretion to the interpretation of the contrary effect—the *negative* variation—in the entering skin and lingual rest current (frog). He starts with the assumption that the skin glands are normally “nearly closed to the external surface, *i.e.* have no external galvanic relation.” If during excitation a sudden compression of the liquid contents sets up a deflection of the ingoing current in the glandular epithelium, then—under the further presumption of a homodromous, electromotive activity of the remaining epithelium—“the relation of E.M.F. between glandular skin and epithelium” determines the character of the phenomena of excitation.

If the first is greater, a *positive* increment of the rest current appears, an “ingoing secretion current.” “If the E.M.F. of the gland epithelium, on the contrary, is less than that of the skin epithelium, as must be presumed in the resting state of the glands, the mere mechanical process of secretion will produce a diminution of the rest current, followed however by augmentation, so soon as the excitation of the nerve incites the cells to secretory activity.” Notwithstanding Hermann’s recent protest (82), we continue to hold this explanation fallacious, and are still of opinion that the conditions of leading off are similar to those in the frog’s tongue.

The electromotive action of the mucosa of the stomach claims attention both on theoretical grounds, and in regard to the disputed question as to the existence of special secretory nerves to the glands. We found above, as first stated by Rosenthal (73), that the mucous coat of the frog’s stomach had normally the same electromotive action as the outer skin of fishes and naked amphibia, *i.e.* on leading off from the free internal surface and muscular coat a powerful ingoing current is exhibited, which Rosenthal does not hesitate to connect with the mucous glands. Yet in view of the facts discussed above we must admit another possibility, *viz.* that the whole surface epithelium may consist of elements, which are to be regarded as unicellular mucous glands

in the same sense as the goblet cells of throat or cloacal mucosa, or the gland cells of the frog's tongue. These being incontestably electrically active, we may affirm with almost positive certainty that—granting the glands of the stomach proper to possess electrical action—the ingoing mucous current must consist of at least two components.

In order to decide this question, F. Bohlen (84) carried out under our direction a series of experiments (on the frog in the first instance), the object of which was to demonstrate the influence of the digestive activities of the stomach upon its electromotive properties. If these really depended on the gastric glands, we should expect to find considerable alterations in the fasting state, *vs.* state of digestion. This proved to be the case, but not, as was expected, in the sense of augmentation of the “current of rest” in the replete animal, but on the contrary of a marked diminution. Only when *indigestible* substances, such as stones, wood, etc., which excite the mucosa *mechanically*, were introduced into the stomach, an often considerable increase of the normal, ingoing current became perceptible, together with increase of mucous secretion. This was to a marked degree the case after the introduction of bismuth subnitrate, where the sharp-edged crystals seemed to act as an intense stimulus, and produced a quite specific mucous secretion. When the insoluble salt reaches the cloaca, it causes a marked secretion of mucin, and a corresponding augmentation of the electrical current, so that—as in the stomach—the scale flies beyond the field of vision. For the rest, the E.M.F. of the mucosa of the stomach is conditioned, as in other secreting membranes referred to (which secrete *mucin only*), by a variety of factors: in particular, temperature, dehydration and turgor, anæsthesia, etc. Direct electrical excitation by rapidly alternating shocks from an induction coil effects at a small distance of coil a negative variation, usually preceded by a positive swing. The strength of the original current is therefore of essential significance, since the deflection corresponding with the negative variation is, so to speak, in direct ratio with the E.M.F. of the preparation.

In warm-blooded animals also (rabbit, guinea-pig, rat) Bohlen ascertained the existence of a vigorous ingoing current. After opening the belly, an unpolarisable tube electrode closed with a clay stopper was passed through a hole in the wall of the

stomach, the other being in contact with the external surface of the stomach. This in rabbits and guinea-pigs is nearly always crammed with food, so that the lead-off from the mucosa is here complicated by the contents of the stomach, which suggests certain objections. In the first place, one asks whether warmth may not have a perceptible effect on the electrode inserted deep into the stomach; in the second, differences of potential are caused by the contents of the stomach, so that the results of the observation are disturbed to an extent which it is impossible to calculate.

In regard to the first question, it is easy to see that the currents caused by differences of temperature do not come into the reckoning at all, in comparison with the marked effects of the physiological mucosa current. The second question is solved by the fact that almost directly after the death of the animal there is a decline of E.M.F. which soon tends to reversal of the current, but this current appears in the same way and at the same intensity whether the stomach is emptied and washed, and then led off directly from the surface of the mucosa, or whether it is already empty, *e.g.* in rats that have been kept without food for some days.

In warm-blooded animals, as in the frog, the intensity of the rest current varies in individual cases, within a certain range. Sometimes, nearly always indeed, it is so strong that the scale flies far off the field; in other cases again only deflections of a few degrees are visible. Oscillations occur almost invariably, which are of very different magnitudes.

The effect of deep narcosis upon the strength of the current in the mucosa of the stomach is very striking in mammals. With a little care in the use of chloroform and ether, the variation can be diminished until the deflection barely reaches 10 degrees of the scale. A long period must then elapse before the current returns to its original magnitude. Whether this is a direct or indirect effect is foreign to our present discussion.

As in the frog, so in warm-blooded animals, the E.M.F. of the mucosa is considerably heightened by the introduction of bismuth (2-5 grs. in emulsion), along with which there is an easily-confirmed increase in the mucin secretion.

Artificial excitation of the vagus nerve produces striking consequences. While the only result in the frog is a weak, positive

variation of the entering current, which appears whether the stomach is excised or *in situ*,—in mammals, after a transitory increase of the entering current, there regularly appears a negative variation which can reach such proportions that the current not only sinks to zero, but goes beyond it in the reversed direction, so that the now outgoing current may, under certain conditions, become as strong as the original ingoing current. That this is not, as might have been supposed, an action of secretory nerves, but merely an after-manifestation of the disturbance of the circulation due to the slowing or stand-still of the heart, and, in the first degree, to the marked *fall of blood-pressure*, is very easily determined. It appears not merely from the time coincidence of the latter and the negative variation, but more particularly from the fact that whatever depresses blood-pressure locally or in general, also tends to diminish the ingoing current of the stomach. This applies to every severe loss of blood, and notably still more where clamping of the aorta has temporarily produced a complete anæmia of the stomach. The current diminishes almost at the moment when anæmia sets in, just as with vagus excitation, to recover again when the blood-stream is freed. Here, as in the first case, it makes no difference whether the vagi have previously been divided at the neck or not. Slow, rhythmical compression and release of the aorta—as best effected by cutting away some of the ribs on the curarised, artificially breathing animal—produce similar rhythmical variations of the stomach current. Every protracted anæmia of the mucosa retards the increase of the current very considerably, until finally recovery is no longer possible. In dyspnœa too, a marked negative swing always follows upon the temporary increase of normal electrical action. The simultaneous tracing of the blood-pressure on the kymograph after double vagus section, proves that there is no immediate coincidence between the alterations of the arterial mean pressure in the carotid and the variations of current, since the negative phase is usually developed at the beginning of the dyspnœic increase of pressure, and continues after blood-pressure has returned to its normal height by renewal of artificial respiration. The positive variation, on the contrary, occurs between the beginning of dyspnœa and the first increase of pressure. It is obvious that this reaction cannot be forthwith interpreted in the sense that the progressive venosity of the blood caused the fall of

the current, for when the vaso-motor centre is excited, and the pressure in the aorta rises, in consequence of dyspnœa, the natural concomitant is fall of pressure in the small arteries and capillaries of many peripheral organs, and the stomach in particular, where, as well as in the viscera, the vessels are narrowest. Similar results are obtained with another experiment on the rabbit, in which, by clamping the four arteries which supply the head, by S. Mayer's method (85), cerebral anæmia is induced with a consequent marked increase of aortic pressure. Here, as during dyspnœic excitation of the vaso-motor centres, the stomach current again—after a brief positive fore-swing—declines very markedly, being as a rule *already reversed at a time when the blood-pressure is at its maximum*. If the clip is removed before the centre has become permanently injured, the blood-pressure returns rapidly to its normal level, but the current requires much longer to recover its original proportions. If, on the other hand, anæmia is prolonged till the blood-pressure is at "paralytic" level, owing to the paralysis of the centre, the ingoing direction of the current does indeed gradually reassert itself, but never approximates to its original strength, exhibiting at most a deflection of a few gradations.

In view of the last-named results, in which venous action of the blood passing into the stomach of the slightly curarised, artificially breathing animal seems to be wholly excluded, the presumption gains ground that local decline of pressure in consequence of diminished arterial blood-supply is in dyspnœa also the proper cause of the negative variation. We should then expect an opposite effect, *i.e. increase* of entering current, when pressure was raised in the vascular system. One way in which this can be accomplished is by *transfusion of fluids at greater densities*. It is known from the investigations of Cohnheim and Lichtheim (86) that even when enormous quantities of 0.6 % salt solution is injected into the jugular vein of rabbit or dog, the blood-pressure undergoes no particular increase, and remains fairly normal. "There was no question of rise in ratio with the densities injected. Marked increase of pressure only occurred during an experiment when the initial pressure had been excessively low; in this case the infusion of fluid produced rapid rise of blood-pressure to the mean." On the other hand, a marked *acceleration of the circulation* was obvious in all these experiments,

even under the microscope. There was also an extraordinary increase of bulk of water in the blood, producing fundamental disturbances of nutrition in the tissues, as exhibited *inter alia* by the appearance of rich transudations in different organs, more particularly in the abdominal intestinal tract. The former, as found by Cohnheim and Lichtheim, discharged a large bulk of fluid after each plentiful infusion of salt solution, while the mucosa often swells to a thickness of 2 cm., and the intestine appears full of exuded matter.

A marked augmentation of the entering abdominal current is nearly always exhibited in the rabbit shortly after the commencement of infusion with salt solution, increasing more and more as the experiment progresses, and finally reaching such abnormal proportions that the galvanometer mirror is driven off the field even when the current has already been compensated. It is noticeable that in these cases a marked ingoing current may be observed for a long time after the death of the animal, which never occurs under normal relations.

The significance of these, as of the other experiments described, can only be indicated in a later connection. Here we can only state that the fundamental conformity in electromotive properties existing between the mucosa of the frog's stomach, and that of the tongue, throat, and cloaca, and especially the fact that all circumstances producing mucous secretion tend to increase the entering current, give decisive evidence that the electromotive effects depend, if not solely, at least in the first degree, upon the mucin-secreting elements of the stomach, *i.e.* its surface epithelium. Whether, and how far, the actual secreting glands are concerned in it, may perhaps be decided from a more detailed examination of the changes in electromotive action which accompany the digestive processes in warm-blooded animals.

In any case there is not the slightest ground for making the peptic glands of the stomach alone responsible for the current of the mucosa; the less so, since there is regularly a very significant quantitative difference in electromotive action between the stomach and intestine, which would be unintelligible if—as would then be assumed—the many glands of the intestinal mucosa were as electrically active as the glands of the stomach. On the other hand, the difference is easily understood if we

consider the small number of mucin-producing goblet cells in the one case, and the continuous surface layer of the same in the other.

We are of opinion that the preceding observations leave no doubt that the electromotive effects described in certain mucosæ, and in the external skin of naked amphibians and fishes, are to be referred to the greater or less number of uni- and multicellular secreting glands present, *i.e.*, in the last resort, to the single cell.

From the standpoint of the earlier theoretical account of electromotive action it is evident that, as regards the explanation of the "ingoing current of rest," no difficulty is encountered. Every goblet cell, or mucous cell proper, exhibits, as a rule, under the microscope two clearly distinguishable sections—one basal, nucleated and protoplasmic—the other dimmed, as a rule, by a mass of granules, but on treatment with reagents becoming hyaline and turgescient, *i.e.* exhibiting unmistakable mucin metamorphosis. It must be concluded that "chemical action" in the two parts of the same cell differs not only quantitatively but qualitatively also, which explains the difference of potential between base and free surface, fundamental to the ingoing current, if the mucin metamorphosis is admitted to be a chemical process, developing *pari passu* with the negative potential. This naturally applies as much to simple, superficially extended cell aggregates (throat and cloacal mucosa, external skin of many fishes) as to the cases in which there is a more or less complex pitting (glandular formation); for it is clear that, inasmuch as these glands open to the exterior, part of their current must be included in the lead-off, which would naturally be "ingoing," like the current of the superficial mucous cells. The usually higher E.M.F. of the richly glandular mucosa (tongue) and frog's skin, *vs.* the fish's skin, consisting only of goblet cells, and the throat and cloacal mucosa, may well be referred to this fact; for there is no reason to suppose that the sparsely present goblet cells, still less the prickle cells of the frog's epidermis, have any such important electrical action. If, as pointed out by Hermann, the form of the glands in the frog's skin is but little suited to give external galvanic action, on the other hand the capillary layer of fluid which covers the surface of the skin under normal conditions, and must be regarded mainly as a glandular secretion, is directly connected with the fluid contents of the

glands, and so makes a lead-off possible. In the tongue, at all events, this is certainly the case. It was said above that the other reasons, in particular the experiments of Bach and Oehler on the corroded skin, which Hermann brings forward against the participation of the glands in the skin "rest current," are by no means conclusive. At any rate, it cannot be denied that the surface epithelium does contribute to the rest current—the more so, since recent experiments have demonstrated electromotive effects in skin that is perfectly free of glands (88). If, in view of Hermann's theory of the cause of the entering skin and mucosa currents, it was desired to predict the effect most likely to ensue with direct or indirect excitation, the *positive* variation, *i.e.* augmentation of the rest current, would inevitably be selected, and explained by the processes of alteration in the glandular epithelium strengthened or perhaps initiated by excitation. But from the above it appears that the exact contrary is the case—the *negative* variation is more and more the exclusive consequence of excitation, in proportion with the E.M.F. of the entering rest current.

And that the latter itself cannot be explained by the above simple hypothesis is quite evident from the reactions described with energetic cooling. It should here be noted more especially that in this respect the complicated, richly glandular objects (tongue) coincide with the most simply constructed (throat and cloacal mucosa), so that there can be no question of referring the opposite electrical effects before and after cooling, to any anatomical difference in the elements. Hence no other conclusion is possible but that *the same epithelial cell, almost to the same degree, is able to give electromotive response now in the one direction and now in the other.* In this, as in many other respects, the cell current in question differs fundamentally from the electrical manifestations of nerve and muscle. In these the strongest cooling at most produces diminution, never, however, reversal of the demarcation current. This is a good instance of how little the galvanometer is able to indicate the quality of the chemical process which in both cases underlies the homodromous differences of potential. As Hering aptly remarks, it can only express "alterations and differences of chemical action in the different parts of a living continuum, together with the magnitude and time relations of such action."

Many of these manifestations, in particular the frequent alternation in direction of the deflections, which appears spontaneously without any demonstrable cause, sometimes also rhythmically, seem to indicate that *each cell is to be regarded as the seat of two distinct chemical processes, which—existing simultaneously—produce heterodromous potentials. The observed deflection would therefore always be the sum of two antagonistic forces.*

In order to explain the rapid diminution and final reversal of the normal ingoing current of the skin and mucosa after cooling, we must assume that one of the two current-generating processes (that indeed which implies the development of negative potential) is injured earlier, and to a greater degree, by cold, than the other, so that an outgoing current results from the preponderance of the latter, which in turn gives way to an ingoing current so soon as the normal conditions are restored by heating. The "negative process" appears to be less resistant to other effects also than the "positive." Thus, as we have seen, the suitable abstraction of water will also revive the entering current; on the other hand, lack of oxygen, or treatment with CO_2 , or anæsthetising substances (alcohol, ether, chloroform) impair to the same extent, and eventually abolish, both current-generating processes. In this respect again the perfectly different behaviour of nerve and muscle currents should be noted, in which under these last conditions the diminution is relatively late in appearing.

It is not possible at this juncture to say anything as to the precise nature of these chemical processes in the secretory cells, although one is tempted to conjecture the secretion of water on the one hand, and organic specific secretory constituents on the other. And in favour of this view it might be added, that the entering cloacal current is always strongest when the mucosa is most richly covered with watery secretion, and that while the negative potential of the surface generally increases with the bulk of water present, it rapidly diminishes with loss of water.

This same interpretation also found unlooked-for support in the experiments described above on the mammalian stomach.

The extraordinary influence of changes in blood-pressure on the magnitude of E.M.F. in the abdominal mucosa are at any rate to be referred to this explanation. There can be no doubt that the secretion of water by glandular organs, apart from other

influences, does depend essentially on the actual pressure, and it is at first sight surprising that in the frog neither vagus excitation, nor complete abolition of circulation, produces any such effect on the electromotive properties of the stomach as is proved to be the case in mammals, when a relatively low fall of pressure in the abdominal vessels produces a marked negative variation of the ingoing current. Yet this is intelligible in view of the extraordinary resistance of the frog's skin to all injuries whatsoever. Accordingly, if decrease of pressure in the vessels of the abdominal mucosa is unfavourable to the secretion of water, a negative variation must follow, if—as we are justified in supposing—the actual difference of potential is the sum of two antagonistic electromotive processes, one of which gets the upper hand; as soon as any current manifests itself. And this appears, *inter alia*, from the circumstance that the death of the animal from any cause whatever, is followed under normal conditions by a rapid decline and subsequent reversal of the current. So that the decrease of blood-pressure in warm-blooded animals seems to work like marked cooling upon the mucous glands of the cold-blooded, inasmuch as—if the expression is legitimate—the negative in both cases declines more quickly than the opposite positive process. From this point of view it is easy to explain, not merely the coincidence of result in vagus excitation, marked loss of blood, and diminished blood-pressure due to any poison (amyl nitrite, pilocarpin, chloral, curare, etc.), but also the later effects of dyspnoëic, or anæmic, excitation of the cerebral vaso-motor centres.

Further confirmation of the view thus laid down *re* the effective cause of the normal, ingoing, abdominal current, appears from the results of infusion of salt solution. Here the occasionally enormous secretion of water by the mucosa of the stomach may be directly observed, and when—as frequently happens—there is, notwithstanding the pronounced dilution of the blood and consequent malnutrition of the tissues, a marked increase of electromotive action in the mucosa in the sense of the normal ingoing current, the only explanation possible in the last resort is that the observed differences of potential, and increased secretion of water, are in causative relation.

Bayliss and Bradford (87) previously came to the same conclusions with regard to dependence of electromotive action in the salivary glands on the nature of the secretion.

They appear to have succeeded in the demonstration attempted by Hermann and Luchsinger (79), of the secretion currents in these glands. During rest the surface of the exposed submaxillary gland of the dog was, as a rule, negative to the hilus. The E.M.F. of this current of rest, which must be referred, not to the injured region (muscles), but to the gland itself, varies within a wide range in different individuals, as also in the same animal at different times. The altering relations within the gland would seem to be the cause of this—as is attested by the fact that permanent changes of the current of rest are induced not merely by temporary excitation of the gland nerves, but also by atropin poisoning. The direction of the rest current varies much more (being indeed frequently reversed) in the submaxillary of the cat than in the dog (surface positive to hilus). This is the more striking, in view of the extensive morphological coincidence of this gland in the two animals, since the rest current of the “serous” parotid gland in the dog generally agrees in direction with that of its submaxillary.

Hence it would appear that functional differences in the glands regulate the observed differences of potential. The behaviour of the “action current” on exciting the secretory nerve also speaks for the same conclusion. After compensating the current of rest, excitation of the chorda tympani in the dog always causes negativity of the external surface of the submaxillary gland. The period of this variation is often interrupted by a second antagonistic phase, which sometimes expresses itself only in a retardation or temporary stand-still of the deflection, while it is frequently masked altogether by the first and more pronounced principal phase. The deflection begins after a short latent period, before any secretion has appeared in the canal, and where the excitation is weak it forms the only manifestation.

Excitation of the cervical sympathetic also invariably produces electromotive action in the submaxillary glands of the dog, distinguished, however, from the above by smaller effect, longer latent period, and monophasic variation (surface positive to hilus), *i.e.* the reverse of the principal phase in chorda excitation.

In the same gland of the cat, on the contrary, the second phase (surface positive to hilum) is the more pronounced with excitation from the chorda. Bayliss and Bradford find unmis-

takable relations between the strength of both phases and the nature of the glandular secretion, since it regularly appears that the first phase predominates, or even appears exclusively, where the secretion is plentiful and watery, the second when it is sparse, but rich in mucin. The observed differences in electrical action of the submaxillary in cat and dog respectively would thus be explained by the actual diversity in the secretion yielded in either case on chorda excitation, since in the dog it is much more watery than in the cat.

While in the dog, excitation of the sympathetic only produces an extremely viscid and scanty secretion, in the cat, on the other hand, it is plentiful and watery. The electrical effects are correspondingly small, with prevailing second phase, in the first case—in the second they are considerable, and even exceed the effect of chorda excitation. Bayliss and Bradford consider that poisoning with atropin excludes the action of simultaneous, vaso-motor effects in the electromotive effects observed, since while this drug has no vascular action, it soon abolishes, or very strongly affects, secretory and electrical functions.

Another observation of the same authors on the submaxillary and parotid of the dog must also be noticed. Excitation of the sympathetic, as a rule, produces no quantity of secretion from the last-named gland, yielding only a few drops of viscid submaxillary saliva. Under certain conditions, however, especially after repeated excitation of the cerebral gland nerves, a more plentiful secretion appears, with corresponding alteration of electromotive action. While the surface of both glands is usually positive to the hilus in excitation from the sympathetic, in this instance an opposite variation appears (when the cerebral gland nerves are excited), either alone, or as an accentuated preliminary phase. Bradford is inclined to bring the first electrical change (second phase) into causative relation with the formation of the organic constituents of the saliva, while he refers the opposed, usually stronger, variation to the processes of secretion of water.

If the views thus set forth are legitimate, we should naturally regard both entering and outgoing currents of the glands as "secretion currents," *i.e.* the galvanic expression of permanent chemical action in the secretory cells, and there would be no question of the appearance of a new electromotive force derived

from another source, or other elements, in consequence of *excitation*, but solely of alteration in the galvanic effects of the same elements, which must be regarded during rest as the cause of the differences in potential.

From this point of view, explanation of the actual experimental effects consequent on excitation, presents no serious difficulties, even when complicated double, or multiple, variations are exhibited. Taking first the simple case, where, as in the frog's tongue, a strong ingoing current is present from the beginning, augmentation of the same, *i.e.* a *positive* variation, is only likely to appear when (with direct or indirect excitation) the "negative process" is increased above the "positive," which in the instance cited, where that is already so preponderant, is not very probable; it seems much more likely that the process which is initially less developed should be increased by excitation than the other. From this standpoint it would also be comprehensible that a "*negative* variation" should follow upon excitation, the more exclusively and distinctly in proportion as the original current is stronger. That, further, a positive after-effect frequently makes its appearance, is also intelligible, as soon as it is realised (as proved by experiment) that the positive effect which depends on augmentation of the "negative process" invariably declines much more slowly than the opposite effect, so that when the one has already returned to its normal, the other, from its greater constancy, entails a positive increment of the original current.

The conditions of appearance of a positive variation *during* excitation, either independently or as fore-swing to a subsequent negative variation, are accordingly so much the more favourable in proportion as the homodromous, incoming current is weaker, *i.e.* as the "negative process" is less preponderant. For obviously there is then greater opportunity of strengthening this latter so much by excitation that it in turn becomes uppermost. Strength of the tetanising current is also an important factor, since it would appear that the process leading to development of negative potential at the surface is, under equal conditions, more easily excited than its opposite, so that, as more especially in the mucosa of throat and cloaca, the positive effect appears with weak, the diphasic or single negative effect with stronger, excitation. In particular cases a diphasic effect may of course appear

with many variations, as regards the succession of the two phases. While in the cloaca with a moderately strong entering mucosa current, a positive variation usually precedes the stronger negative effect as a fore-swing, in the mucosa of the throat, under the same conditions, the negative is very frequently interrupted by a positive swing. It is clear that even with complete equality of the two current-generating processes (when currents that can be led off externally are altogether wanting) the possibility of a "secretion current" is not excluded, provided the one or other process is preponderant. Since, in view of the experimental reactions under discussion, this is rather to be expected of the "negative" than of the "positive" process, it is intelligible that positive deflections in the direction of an ingoing current should be visible where the excitation is not too strong. More frequently, however, all galvanic effects of excitation are wanting, from which it must not, of course, be concluded that the secretory process excited by the current is absent, but merely that a particular, physical symptom of the same has in this case not found expression. While, finally, it seems almost self-evident—from the previous argument—that where there is a "reversed" outgoing current in consequence of excitation, there should also be, in an overwhelming majority of cases, deflections of the magnet in the direction of an ingoing current. At all events this is the case almost without exception with weaker excitation, while stronger stimuli, even under these conditions, may still produce a positive variation.

The electromotive action of the skin glands (sweat glands) of mammals and of man is far less exactly determined than in the uni- and multicellular mucous glands. Ever since du Bois-Reymond exhibited his famous experiment (at first referred to the action current of the muscles) on man, in which the lead-off is from both hands or both feet, symmetrically, after which voluntary contraction of one arm, or one leg, deflects the magnet of the multiplier, it was conjectured that this might indicate the development of an entering skin current in consequence of excitation. After Hermann's observations it must be admitted that the action current from the muscles plays no part in it, while if any doubt could still remain on this point, it must finally give way before the experiments of Hermann and Luchsinger on the secretory currents of the cat's skin. As we pointed out in

an earlier connection, du Bois-Reymond's experiment concerns not the *presence* of the secretion, but the *secretory process*, where the visible appearance of sweat is not required.

The same applies in every detail to the pad of the cat's foot, which is rich in sweat-glands. Symmetrical leading-off from the two plantar balls gives, normally, no current of importance, but current is at once produced when the sciatic nerve is cut through on one side. This current is always directed, in the animal, from normal to paralysed side (ingoing). After dividing the second sciatic the difference of potential disappears entirely, to reappear if one or other nerve is artificially excited after curarisation. That this really is a secretion current is proved by the action of atropin—the latency of the galvanic effect is in the first place perceptibly increased, and the intensity of the current declines, and is quickly abolished. On leading off from the undisturbed surface of the exposed muscles and the uninjured epidermis, the incoming current of rest appears to sink on removal of the epithelial layer. "When pilocarpin is injected into one foot, and the lead-off is symmetrical from both feet, there is invariably a strong current from the injected side to the other, *i.e.* increase of entering skin current." Excitation of the central end of the sciatic produces a reflex current from the unexcited to the excited side, where the glands are separated by the division of the nerve from the central organ. The same effect occurs with central excitation of the cruralis (Hermann). The experiment of leading off symmetrically from one paralysed and one non-paralysed foot of a cat sweating freely, either by reason of its struggling, or in the warm chamber, is obviously complementary to du Bois' experiment on man; there cannot be the slightest doubt of its significance, since the current persists under the application of curare, notwithstanding abolition of muscular contraction, while atropin on the other hand neutralises the difference of potential although muscular contraction continues.

An unmistakable secretion, which is demonstrably under nerve-control, is also evident on the skin of the upper lip and nose of the calf, as well as the nostril of sheep and goat. It derives apparently from the large, acinous glands which are seated there. Excitation of the vago-sympathetic always produces increased secretion. So too in the hairless snout of the pig, in which excitation of the peripheral (cephalic) end of

the divided sympathetic discharges large drops of secretion from the openings of the snout glands on the same side. Symmetrical leading-off from two points of the surface then gives a strong ingoing secretion current, with an E.M.F. of possibly 0.07 Dan. The difference of potential in the nose of the goat, and still more, dog or cat, is much less, owing in the last case to the comparative scantiness of the secretion.

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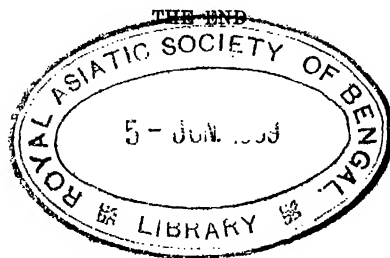
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